U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

130931

SEARCH REQUEST FORM

10780296

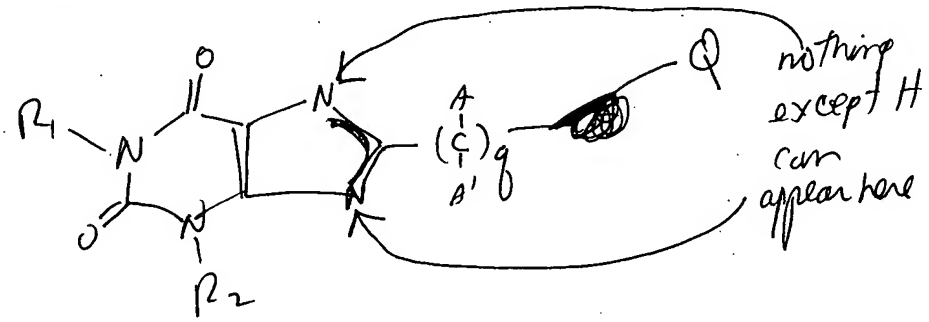
Requestor's Name: BERCH Serial Number: 04/04627

Date: 8/26/04 Phone: 571-272-0663 Art Unit: 1624

Office Rem 5C01 Mailbox 5C18

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).



q = 1-9 r = 1-20

Q = (N/C)-in-a-ring, but the ring must have 5 or 6 members, ring atoms must be O/N/C/S, and at least one bond in ring is other than a single bond

One of R_1, R_2 = $\left(\overset{A}{\underset{A'}{C}}\right)_r - Q$ others is H/C

STAFF USE ONLY

Date completed: _____

Searcher: _____

Terminal time: _____

Elapsed time: _____

CPU time: _____

Total time: _____

Number of Searches: _____

Number of Databases: _____

Search Site

_____ STIC

_____ CM-1

_____ Pre-S

Type of Search

_____ N.A. Sequence

_____ A.A. Sequence

_____ Structure

_____ Bibliographic

Vendors

_____ IG

_____ STN

_____ Dialog

_____ APS

_____ Geninfo

_____ SDC

_____ DARC/Questel

_____ Other

PTO-1590 (9-90)

- I am an examiner in Workgroup: _____ Example: 1610

- *Relevant prior art found, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art not found:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC Biotech Chem Library CM1 – 1C70, Desk

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=> b hcaplus
FILE 'HCAPLUS' ENTERED AT 15:16:21 ON 31 AUG 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 31 Aug 2004  VOL 141 ISS 10
FILE LAST UPDATED: 30 Aug 2004  (20040830/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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L13              STR
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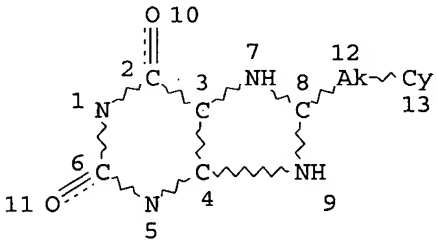


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DEFAULT ECLEVEL IS LIMITED
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NUMBER OF NODES IS  13

STEREO ATTRIBUTES: NONE
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L16          434 SEA FILE=REGISTRY ABB=ON  PLU=ON  L15 AND NR>=4
L17              STR
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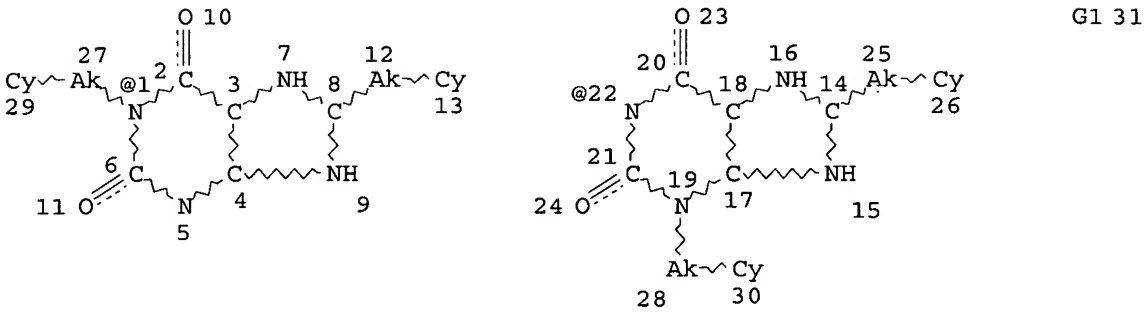

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GRAPH ATTRIBUTES:
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L20 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:1006985 HCAPLUS
DOCUMENT NUMBER: 140:59656
TITLE: Preparation of amide-substituted xanthine derivatives as phosphoenolpyruvate carboxykinase inhibitors with gluconeogenesis modulating activity for treating type 2 diabetes
INVENTOR(S): Dunten, Pete William; Foley, Louise Helen; Huby, Nicholas John Silvester; Pietranico-Cole, Sherrie Lynn; Yun, Weiya
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 191 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003106459	A1	20031224	WO 2003-EP5922	20030605

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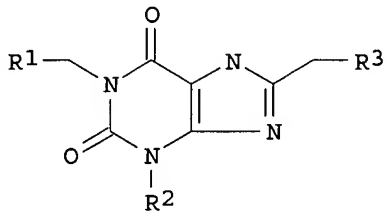
UG, UZ, VN, YU, ZA, ZM, ZW; AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004014766 A1 20040122 US 2003-459944 20030612
PRIORITY APPLN. INFO.: US 2002-388164P P 20020612
US 2003-461010P P 20030407

OTHER SOURCE(S): MARPAT 140:59656

GI



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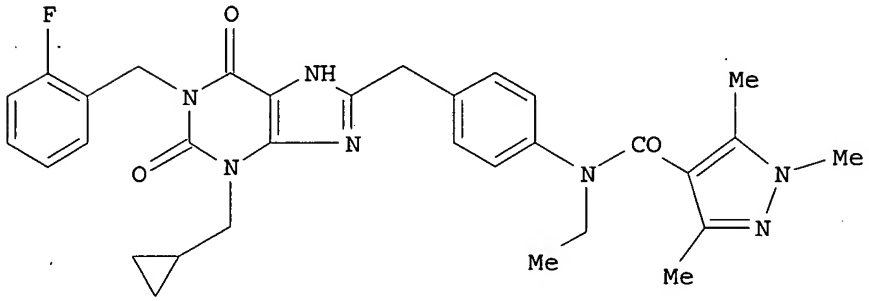


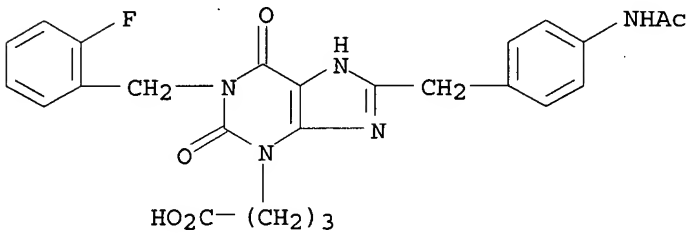
II

AB The present invention comprises 1,3,8 substituted xanthine derivs. (shown as I; variables defined below; e.g. II) or a pharmaceutically acceptable salt thereof. In vitro IC50 values for 37 examples of I are tabulated, e.g. 0.19 μM for II. For I: R1 = lower alkenyl, lower alkynyl, lower alkenyl substituted by halogen, (un)substituted phenyl; R2 = unsubstituted lower alkyl, lower alkyl substituted by lower alkoxy or hydroxy, lower alkenyl, Ph, -(CH2)n-(un)substituted lower cycloalkyl, -(CH2)nC(O)Rb, -(CH2)n-unsubstituted aromatic five-member heterocyclic ring with one O or S, -(CH2)n-aromatic five-member heterocyclic ring with one O or S, the ring substituted by a carboxylic acid moiety, -(CH2)n-unsubstituted aromatic five-member heterocyclic ring with 1-3 N atoms, -(CH2)n-nonarom. five or six member heterocyclic ring with at least one O atom and no or two N atoms, the nonarom. heterocyclic ring having no substituents or having one ring C as a carbonyl. R3 is Re- and Rf-substituted ring wherein 1 ring atom is Q (N or CH, with the proviso that when Q is N), Re is -NHC(O)CH3 and Rf is H and when Q is CH, Re is -NRg-C(O)-Rh, 2-oxopyrrolidin-1-yl or 2-oxoimidazol-1-yl and Rf = H, -NH2 and -NHC(O)CH3; Rg = H, lower alkyl and -(CH2)n-unsubstituted lower cycloalkyl; Rh = -(CH2)n-5-or 6-member aromatic heterocyclic ring having 1-3 hetero atoms independently N, O and S, (un)substituted lower alkyl, -NHRj (Rj = 5- or 6-membered aromatic heterocyclic ring having 1-3 heteroatoms independently N, O and S), -C(O)Rk (Rk = 5- or 6-member aromatic heterocyclic ring having 1-3 hetero atoms independently N, O and S), (un)substituted Ph. T is NH or CH2; n = 0-2; m = 0-1; addnl. details including provisos are given in the claims. A cyclocondensation method of preparation is claimed and 121 example prepns. of I are included. For example, N-[4-[(1-allyl-3-butyl-2,6-dioxo-2,3,6,7-

tetrahydro-1H-purin-8-yl)methyl]phenyl]acetamide was prepared in 6 steps starting from 1-butylurea, Et cyanoacetate and NaOEt and involving intermediates 6-amino-1-butyl-1H-pyrimidine-2,4-dione, 3-allyl-6-amino-1-butyl-1H-pyrimidine-2,4-dione, 3-allyl-6-amino-1-butyl-5-nitroso-1H-pyrimidine-2,4-dione, 3-allyl-5,6-diamino-1-butyl-1H-pyrimidine-2,4-dione, and 2-(4-acetylaminophenyl)-N-(3-allyl-6-amino-1-butyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acetamide; the final step (cyclocondensation) was done in MeOH (11 mL) and 3 N aqueous NaOH (11 mL) at 50° and converted 310 mg of starting material into 190 mg of product.

IT **637335-14-9P 637335-15-0P 637335-16-1P**
637335-23-0P 637335-25-2P 637335-41-2P
637335-43-4P 637335-94-5P 637335-97-8P
637336-02-8P 637336-07-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of amide-substituted xanthine derivs. as phosphoenolpyruvate carboxykinase inhibitors with gluconeogenesis modulating activity for treating type 2 diabetes)

RN 637335-14-9 HCAPLUS
CN 3H-Purine-3-butanoic acid, 8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo- (9CI) (CA INDEX NAME)



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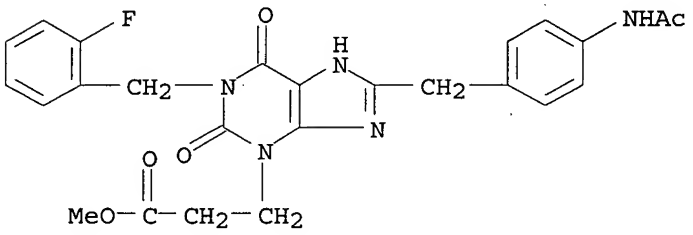
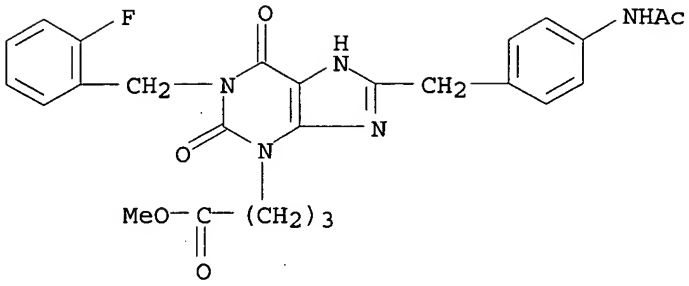
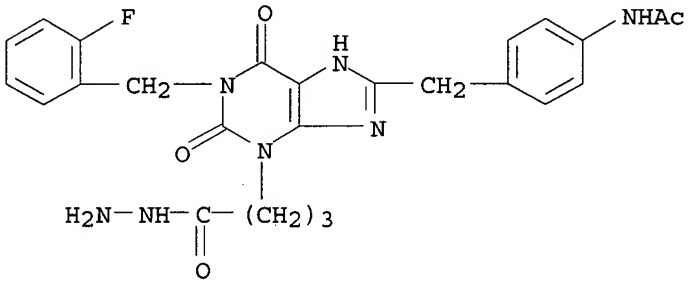
CN 3H-Purine-3-propanoic acid, 8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo-, methyl ester (9CI) (CA INDEX NAME)



RN 637335-16-1 HCAPLUS
CN 3H-Purine-3-butanoic acid, 8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo-, methyl ester (9CI) (CA INDEX NAME)



RN 637335-23-0 HCAPLUS
CN 3H-Purine-3-butanoic acid, 8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo-, hydrazide (9CI) (CA INDEX NAME)



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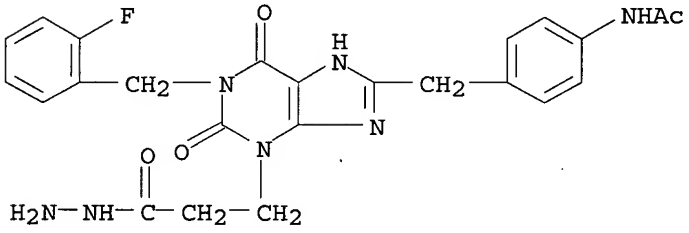
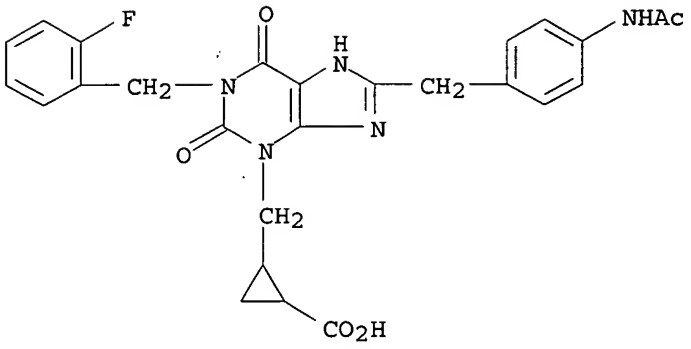
CN 3H-Purine-3-propanoic acid, 8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo-, hydrazide (9CI) (CA INDEX NAME)



RN 637335-41-2 HCAPLUS
CN Cyclopropanecarboxylic acid, 2-[[8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo-3H-purin-3-yl]methyl]- (9CI) (CA INDEX NAME)



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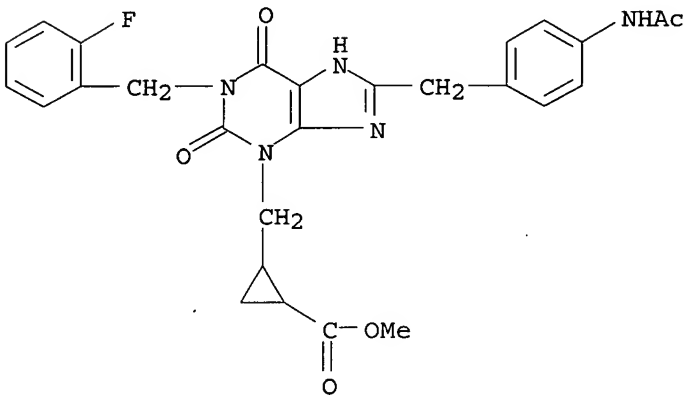
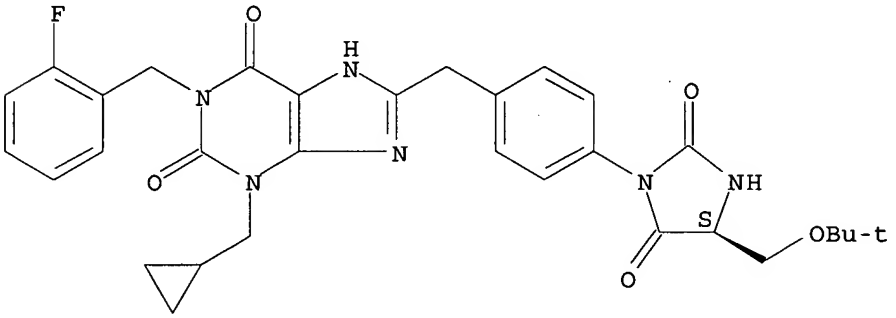
CN Cyclopropanecarboxylic acid, 2-[[8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo-3H-purin-3-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



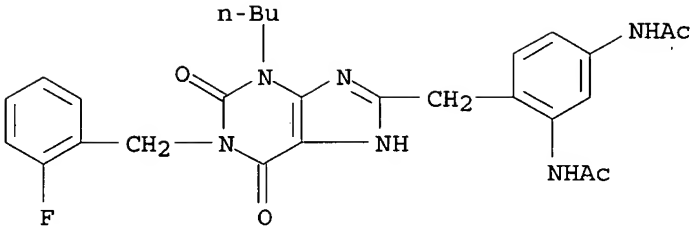
RN 637335-94-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclopropylmethyl)-8-[[4-[(4S)-4-[(1,1-dimethylethoxy)methyl]-2,5-dioxo-1-imidazolidinyl]phenyl]methyl]-1-[(2-fluorophenyl)methyl]-3,7-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



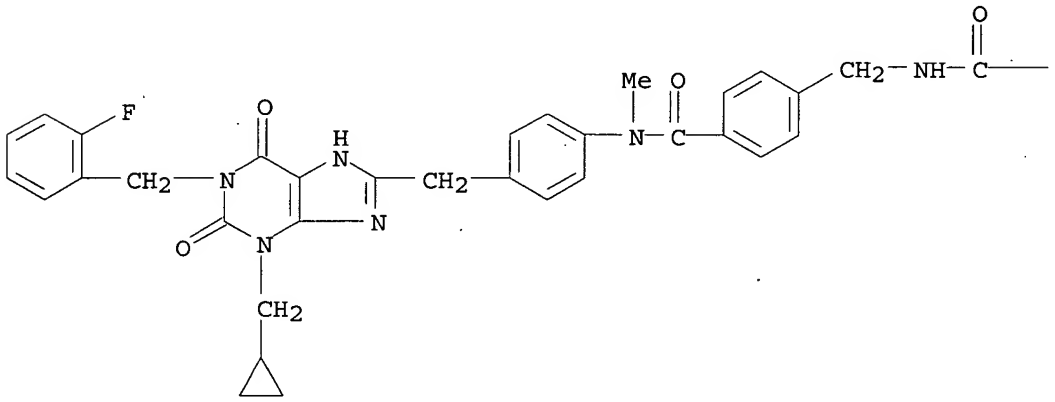
RN 637335-97-8 HCAPLUS
CN Acetamide, N,N'-[4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]-1,3-phenylene]bis- (9CI) (CA INDEX NAME)

Searched by P. Ruppel



RN 637336-02-8 HCAPLUS
CN Carbamic acid, [[4-[[[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]methylamino]carbonyl]phenyl]methyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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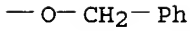

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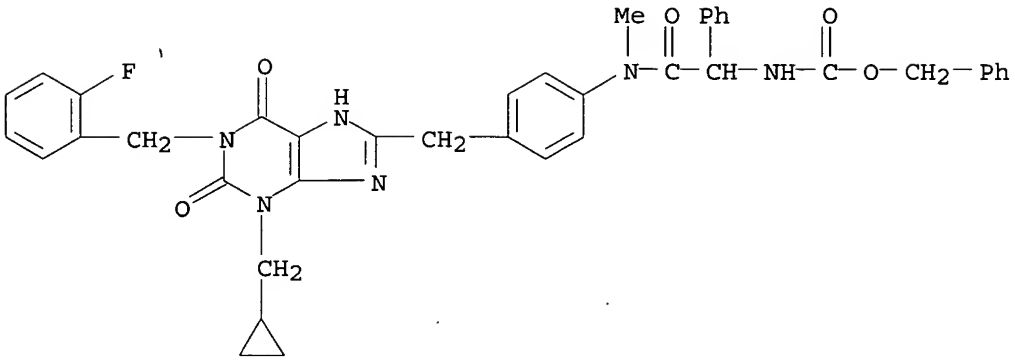

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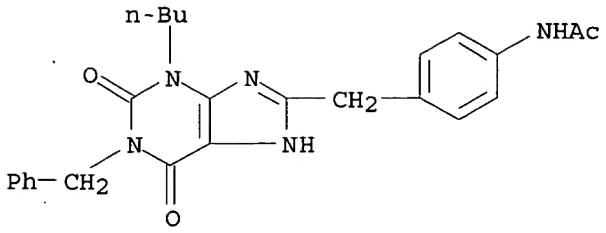
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of amide-substituted xanthine derivs. as phosphoenolpyruvate carboxykinase inhibitors with gluconeogenesis modulating activity for treating type 2 diabetes)

RN 628279-06-1 HCAPLUS

CN Acetamide, N-[4-[[3-butyl-2,3,6,7-tetrahydro-2,6-dioxo-1-(phenylmethyl)-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



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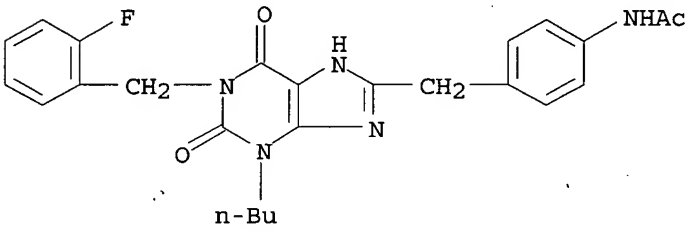
CN Acetamide, N-[4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



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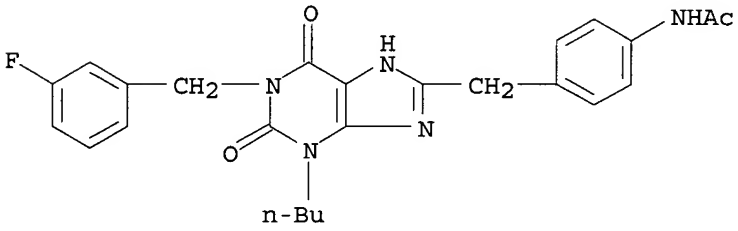

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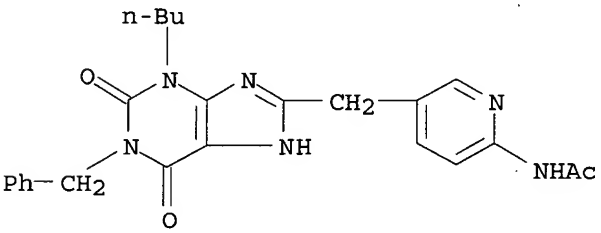
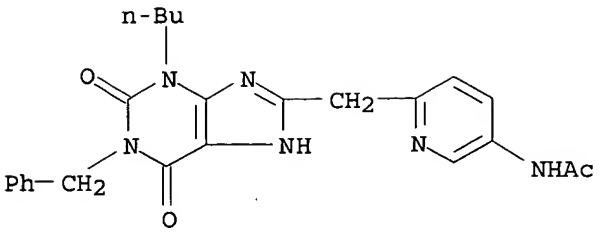
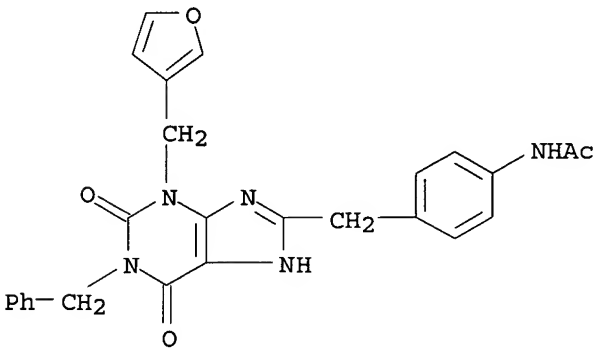


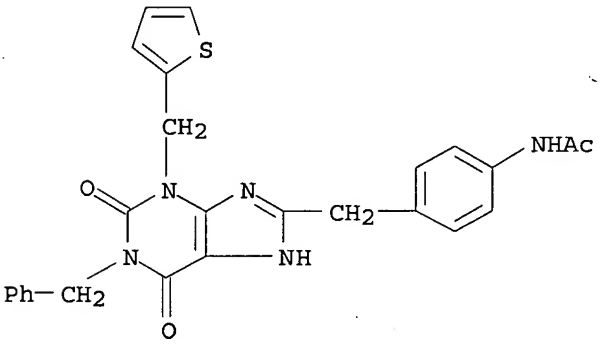
RN 637334-88-4 HCAPLUS
CN Acetamide, N-[6-[[3-butyl-2,3,6,7-tetrahydro-2,6-dioxo-1-(phenylmethyl)-1H-purin-8-yl]methyl]-3-pyridinyl]- (9CI) (CA INDEX NAME)



RN 637334-90-8 HCAPLUS
CN Acetamide, N-[4-[[3-(3-furanylmethyl)-2,3,6,7-tetrahydro-2,6-dioxo-1-(phenylmethyl)-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



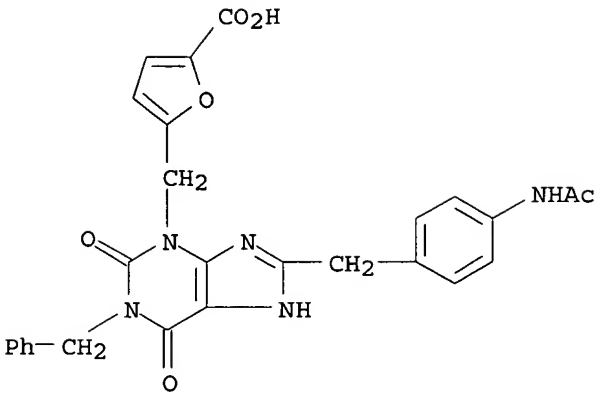
RN 637334-94-2 HCAPLUS
CN Acetamide, N-[4-[[2,3,6,7-tetrahydro-2,6-dioxo-1-(phenylmethyl)-3-(2-thienylmethyl)-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 637334-96-4 HCAPLUS
CN 2-Furancarboxylic acid, 5-[[8-[[4-(acetylamino)phenyl]methyl]-1,2,6,7-tetrahydro-2,6-dioxo-1-(phenylmethyl)-3H-purin-3-yl]methyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

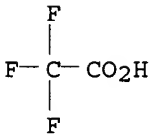
CM 1

CRN 637334-95-3
CMF C27 H23 N5 O6

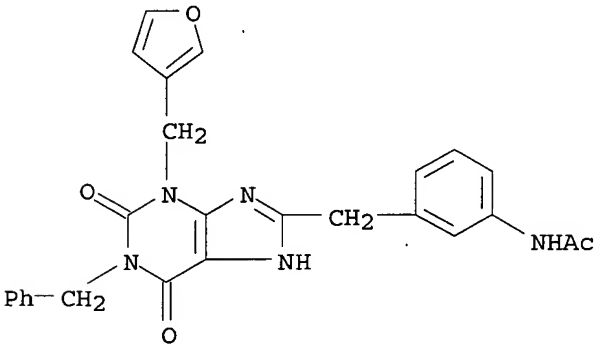


CM 2

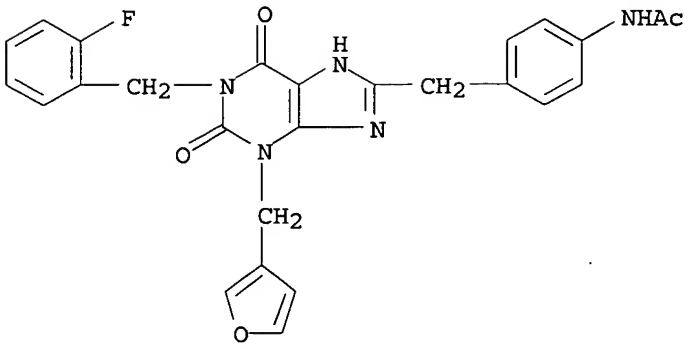
CRN 76-05-1
CMF C2 H F3 O2



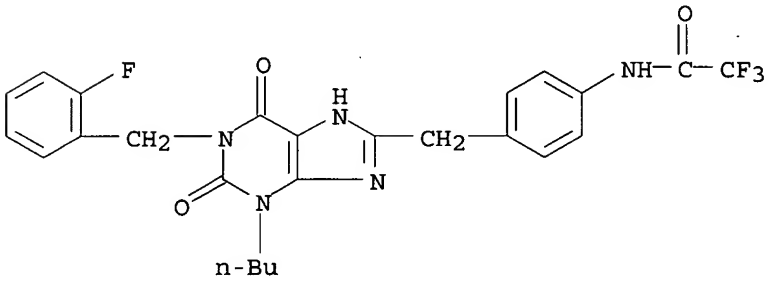
RN 637334-97-5 HCAPLUS
CN Acetamide, N-[3-[[3-(3-furanylmethyl)-2,3,6,7-tetrahydro-2,6-dioxo-1-(phenylmethyl)-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



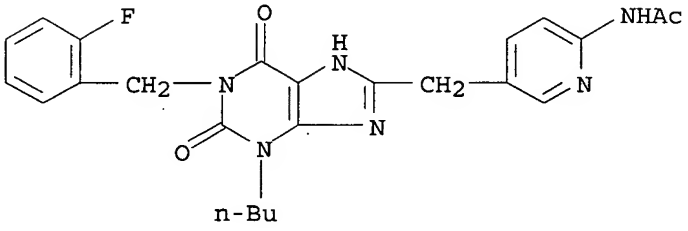
RN 637334-98-6 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-3-(3-furanylmethyl)-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



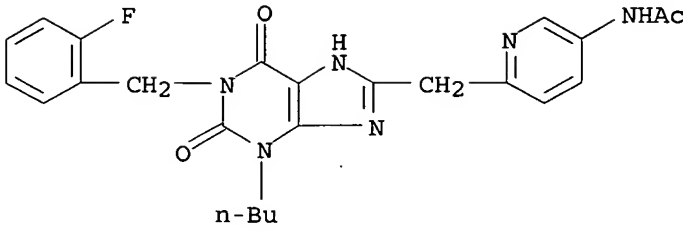
RN 637335-02-5 HCAPLUS
CN Acetamide, N-[4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-2,2,2-trifluoro- (9CI) (CA INDEX NAME)



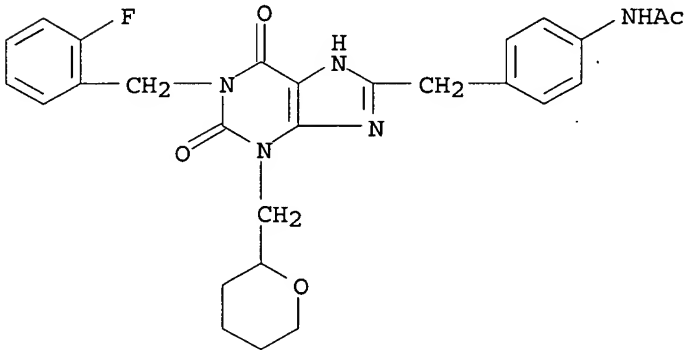
RN 637335-03-6 HCAPLUS
CN Acetamide, N-[5-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]-2-pyridinyl]- (9CI) (CA INDEX NAME)



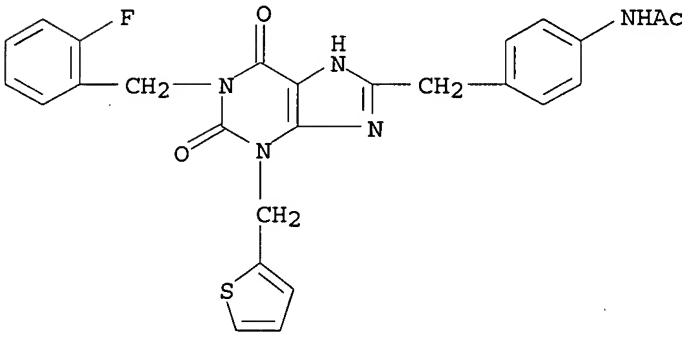
RN 637335-04-7 HCAPLUS
CN Acetamide, N-[6-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]-3-pyridinyl]- (9CI) (CA INDEX NAME)



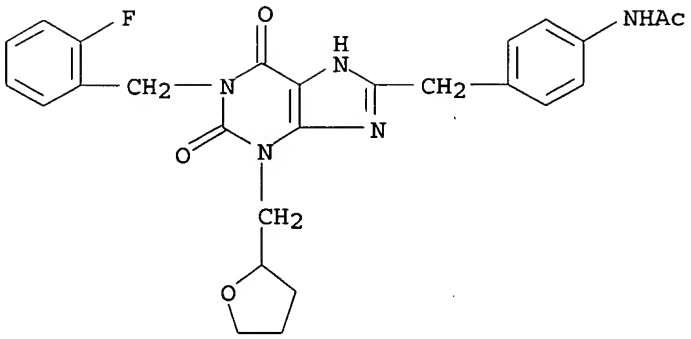
RN 637335-05-8 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-3-[(tetrahydro-2H-pyran-2-yl)methyl]-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 637335-06-9 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-3-(2-thienylmethyl)-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



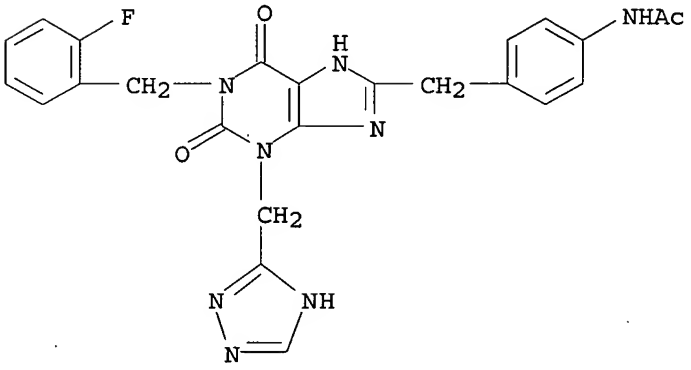
RN 637335-07-0 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-3-[(tetrahydro-2-furanyl)methyl]-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 637335-09-2 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-3-(1H-1,2,4-triazol-3-ylmethyl)-1H-purin-8-yl]methyl]phenyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

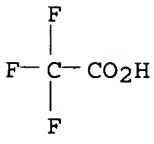
CM 1

CRN 637335-08-1
CMF C24 H21 F N8 O3

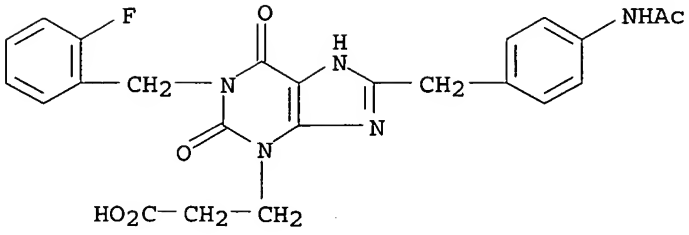


CM 2

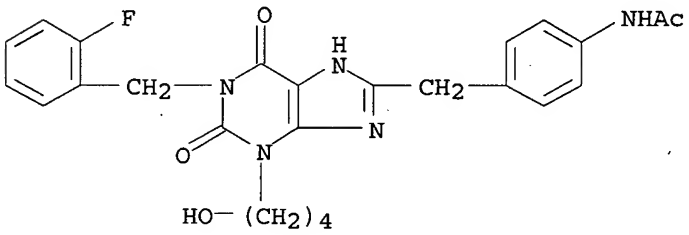
CRN 76-05-1
CMF C2 H F3 O2



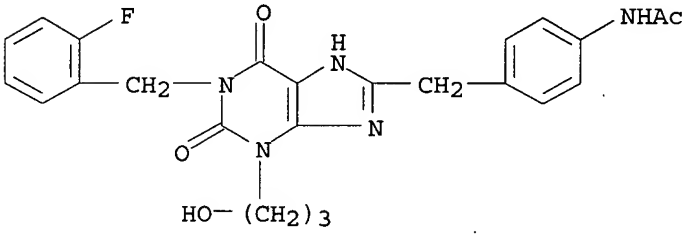
RN 637335-13-8 HCAPLUS
CN 3H-Purine-3-propanoic acid, 8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo- (9CI) (CA INDEX NAME)



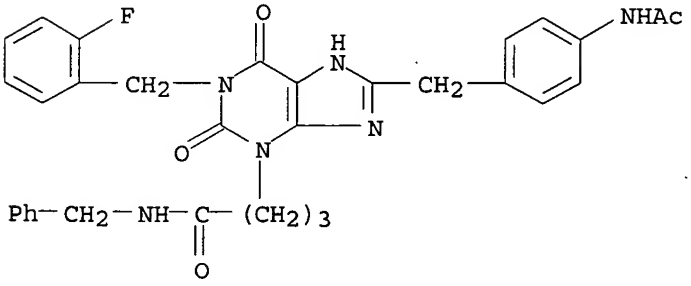
RN 637335-17-2 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-3-(4-hydroxybutyl)-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



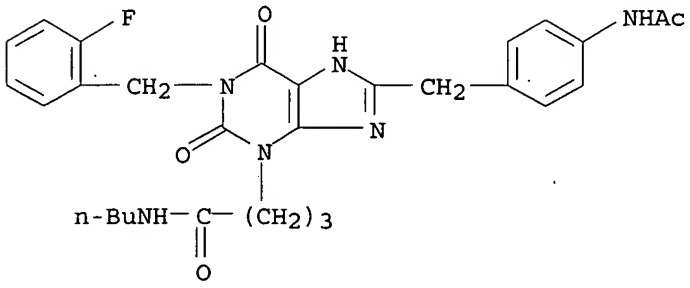
RN 637335-18-3 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-3-(3-hydroxypropyl)-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



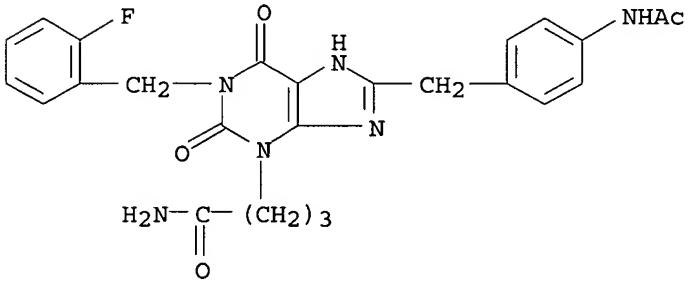
RN 637335-19-4 HCAPLUS
CN 3H-Purine-3-butanamide, 8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



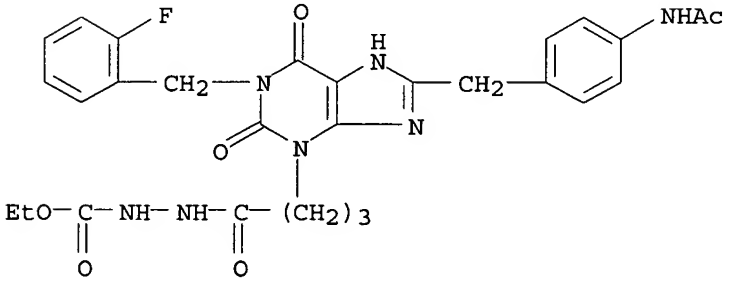
RN 637335-20-7 HCAPLUS
CN 3H-Purine-3-butanamide, 8-[[4-(acetylamino)phenyl]methyl]-N-butyl-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo- (9CI) (CA INDEX NAME)



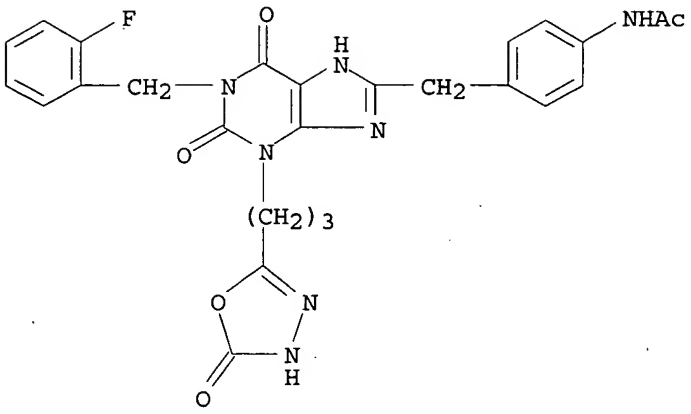
RN 637335-21-8 HCAPLUS
CN 3H-Purine-3-butanamide, 8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo- (9CI) (CA INDEX NAME)



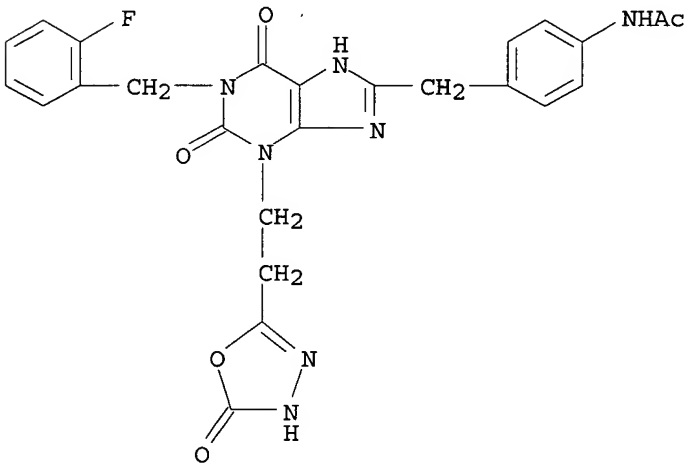
RN 637335-22-9 HCAPLUS
CN 3H-Purine-3-butanoic acid, 8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo-, 2-(ethoxycarbonyl)hydrazide (9CI) (CA INDEX NAME)



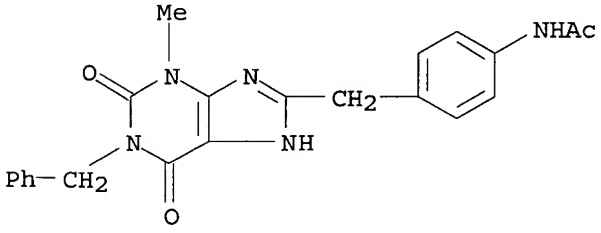
RN 637335-24-1 HCAPLUS
CN Acetamide, N-[4-[[3-[3-(4,5-dihydro-5-oxo-1,3,4-oxadiazol-2-yl)propyl]-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 637335-26-3 HCAPLUS
CN Acetamide, N-[4-[[3-[2-(4,5-dihydro-5-oxo-1,3,4-oxadiazol-2-yl)ethyl]-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)

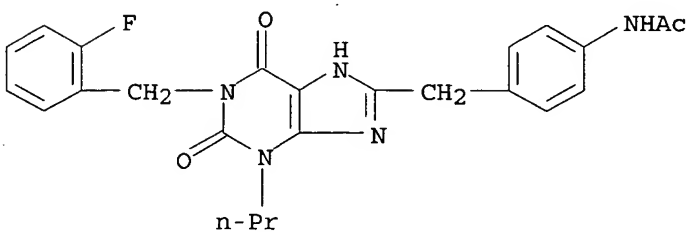


RN 637335-27-4 HCAPLUS
CN Acetamide, N-[4-[[2,3,6,7-tetrahydro-3-methyl-2,6-dioxo-1-(phenylmethyl)-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)

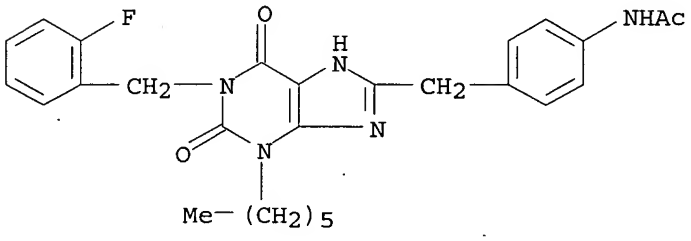


RN 637335-28-5 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-

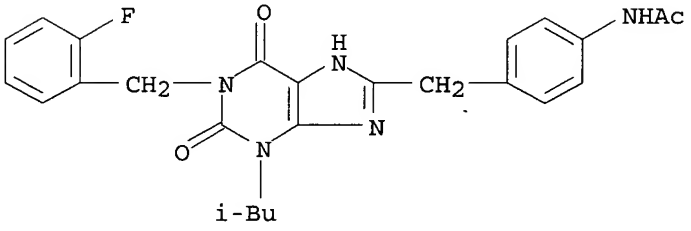
3-propyl-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



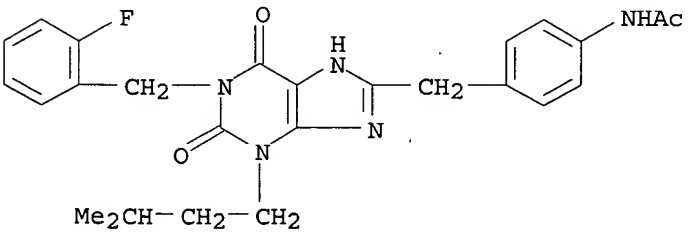
RN 637335-29-6 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-3-hexyl-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



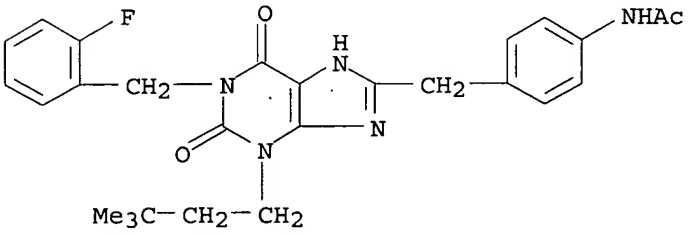
RN 637335-30-9 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-3-(2-methylpropyl)-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



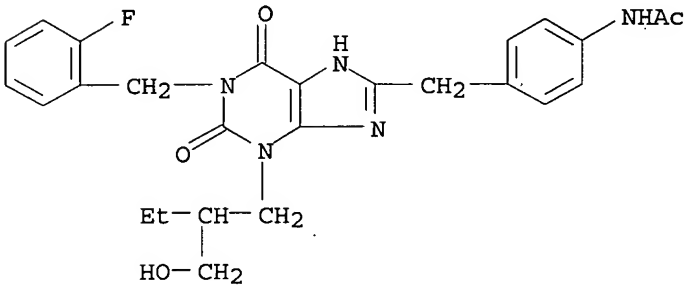
RN 637335-31-0 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-3-(3-methylbutyl)-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



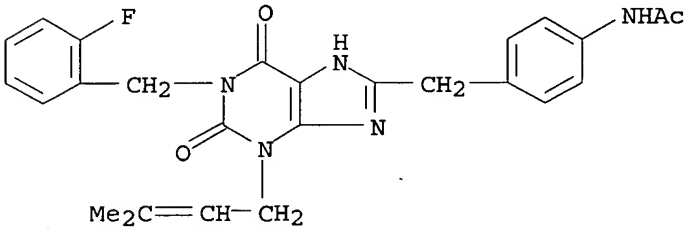
RN 637335-32-1 HCAPLUS
CN Acetamide, N-[4-[[3-(3,3-dimethylbutyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



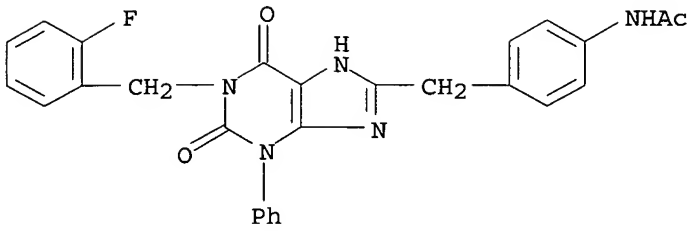
RN 637335-33-2 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-3-[2-(hydroxymethyl)butyl]-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



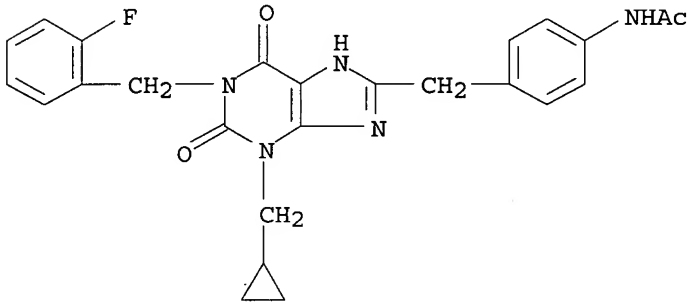
RN 637335-34-3 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-3-(3-methyl-2-butenyl)-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



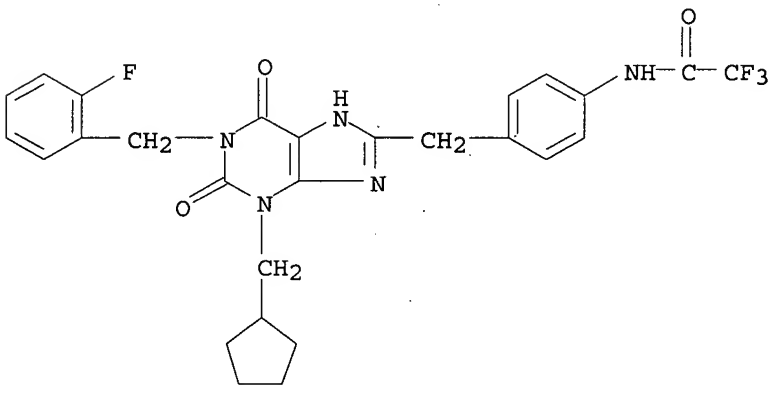
RN 637335-35-4 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-3-phenyl-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



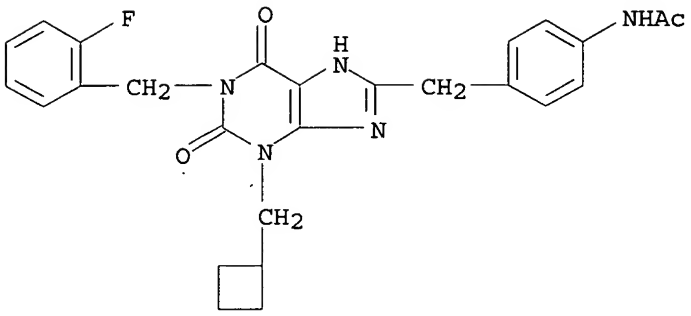
RN 637335-36-5 HCAPLUS
CN Acetamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



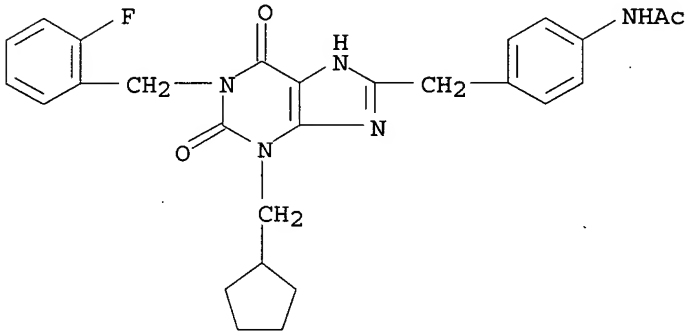
RN 637335-37-6 HCAPLUS
CN Acetamide, N-[4-[[3-(cyclopentylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-2,2,2-trifluoro- (9CI) (CA INDEX NAME)



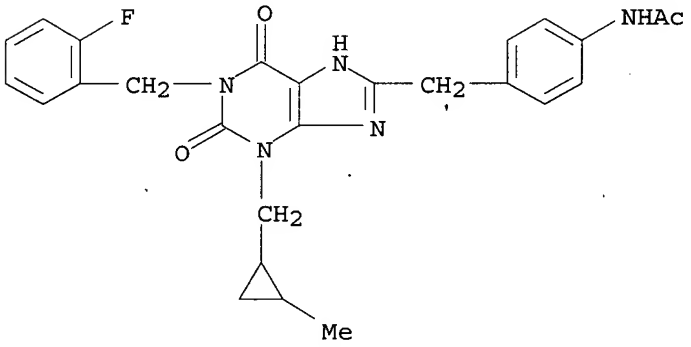
RN 637335-38-7 HCAPLUS
CN Acetamide, N-[4-[[3-(cyclobutylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



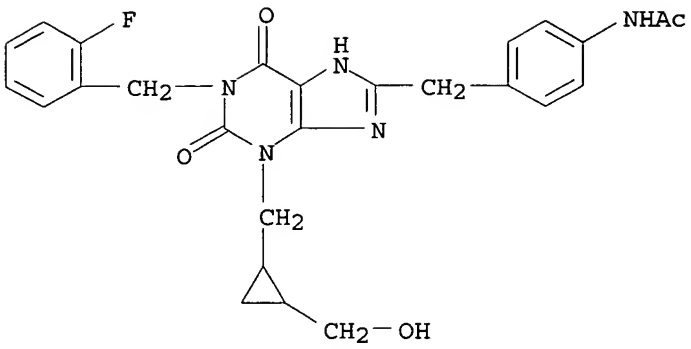
RN 637335-39-8 HCAPLUS
CN Acetamide, N-[4-[[3-(cyclopentylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



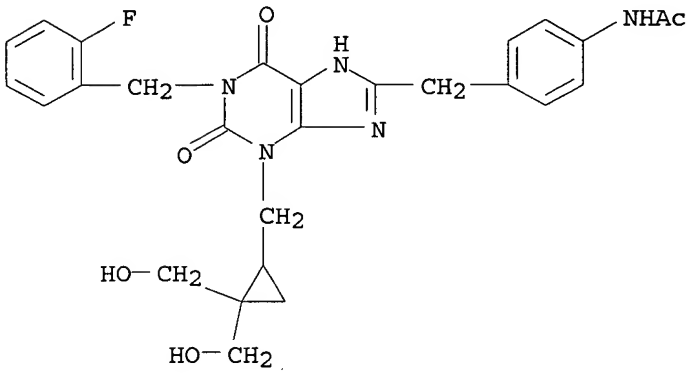
RN 637335-40-1 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-3-[(2-methylcyclopropyl)methyl]-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



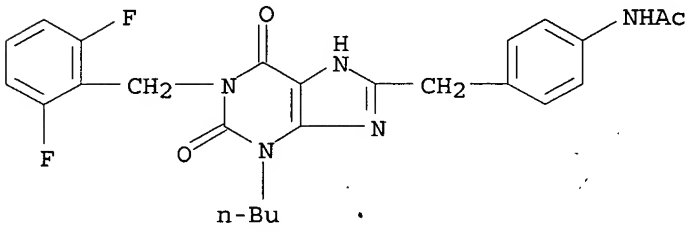
RN 637335-44-5 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-3-[[2-(hydroxymethyl)cyclopropyl]methyl]-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



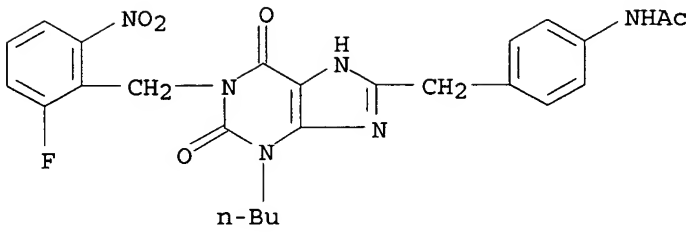
RN 637335-45-6 HCAPLUS
CN Acetamide, N-[4-[[3-[[2,2-bis(hydroxymethyl)cyclopropyl]methyl]-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



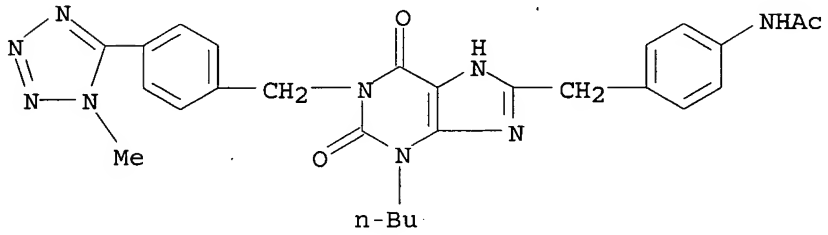
RN 637335-53-6 HCAPLUS
CN Acetamide, N-[4-[[3-butyl-1-[(2,6-difluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 637335-54-7 HCAPLUS
CN Acetamide, N-[4-[[3-butyl-1-[(2-fluoro-6-nitrophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



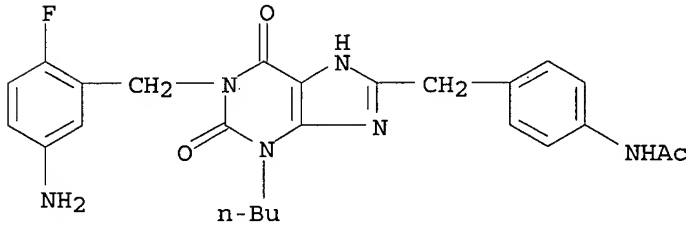
RN 637335-55-8 HCAPLUS
CN Acetamide, N-[4-[[3-butyl-2,3,6,7-tetrahydro-1-[[4-(1-methyl-1H-tetrazol-5-yl)phenyl]methyl]-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 637335-57-0 HCAPLUS
CN Acetamide, N-[4-[[1-[(5-amino-2-fluorophenyl)methyl]-3-butyl-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

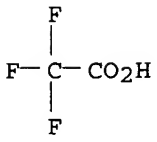
CM 1

CRN 637335-56-9
CMF C25 H27 F N6 O3

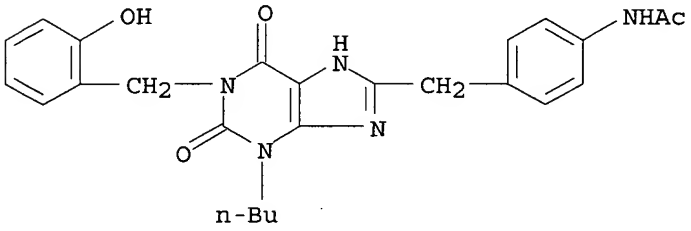


CM 2

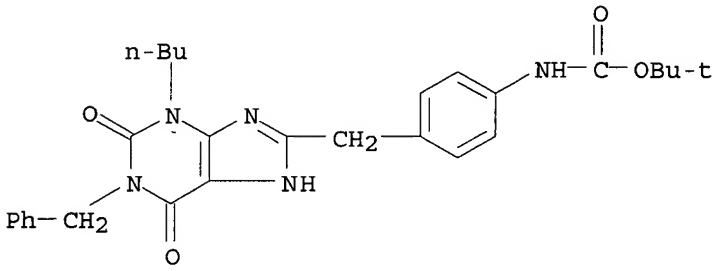
CRN 76-05-1
CMF C2 H F3 O2



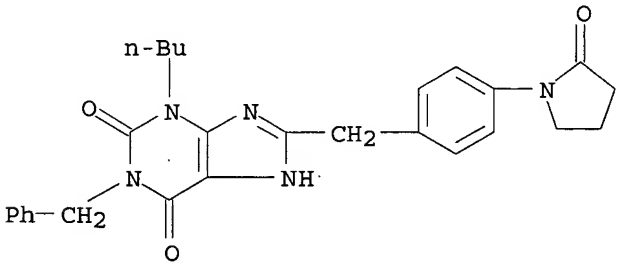
RN 637335-65-0 HCAPLUS
CN Acetamide, N-[4-[[3-butyl-2,3,6,7-tetrahydro-1-[(2-hydroxyphenyl)methyl]-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 637335-68-3 HCAPLUS
CN Carbamic acid, [4-[[3-butyl-2,3,6,7-tetrahydro-2,6-dioxo-1-(phenylmethyl)-1H-purin-8-yl]methyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

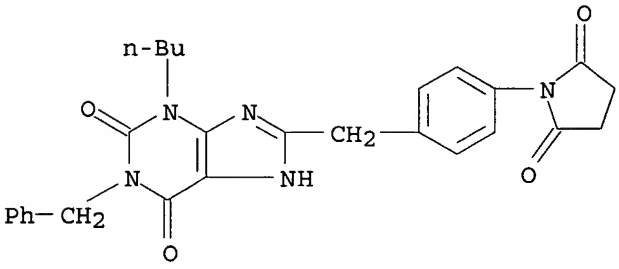


RN 637335-69-4 HCAPLUS
CN 1H-Purine-2,6-dione, 3-butyl-3,7-dihydro-8-[[4-(2-oxo-1-pyrrolidinyl)phenyl]methyl]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 637335-71-8 HCAPLUS
CN 1H-Purine-2,6-dione, 3-butyl-8-[[4-(2,5-dioxo-1-

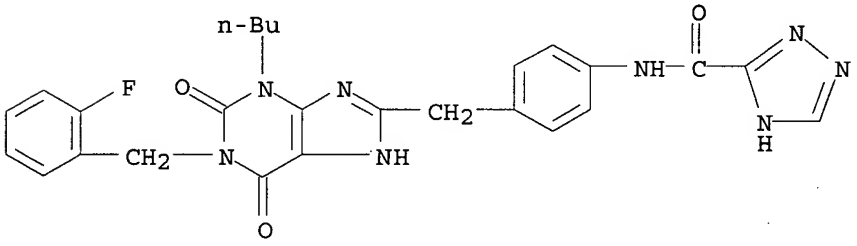
pyrrolidinyl)phenyl]methyl]-3,7-dihydro-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 637335-73-0 HCAPLUS
CN 1H-1,2,4-Triazole-3-carboxamide, N-[4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

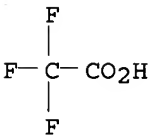
CM 1

CRN 637335-72-9
CMF C26 H25 F N8 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2

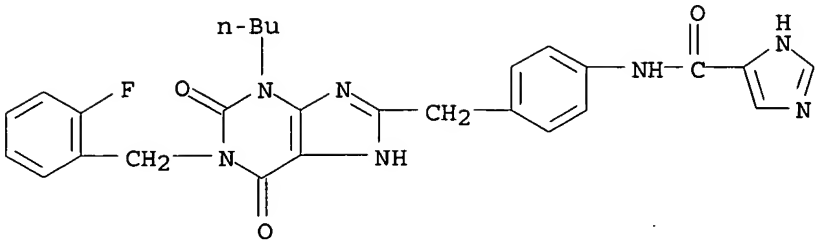


RN 637335-78-5 HCAPLUS
CN 1H-Imidazole-4-carboxamide, N-[4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

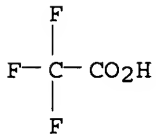
CRN 637335-77-4

CMF C27 H26 F N7 O3

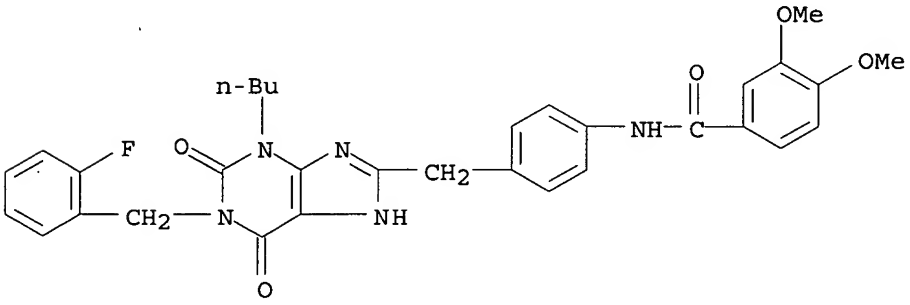


CM 2

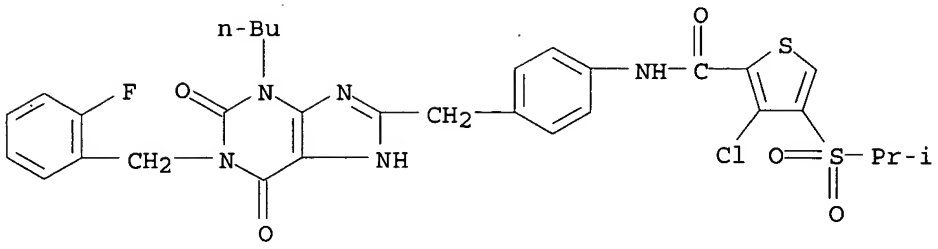
CRN 76-05-1
CMF C2 H F3 O2



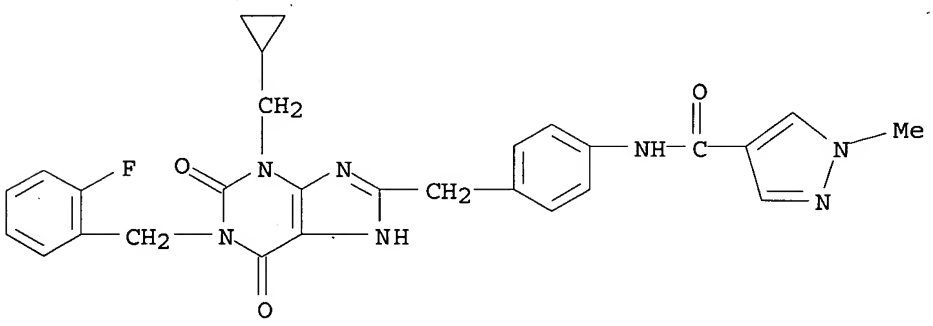
RN 637335-81-0 HCAPLUS
CN Benzamide, N-[4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-3,4-dimethoxy- (9CI) (CA INDEX NAME)



RN 637335-83-2 HCAPLUS
CN 2-Thiophenecarboxamide, N-[4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-3-chloro-4-[(1-methylethyl)sulfonyl]- (9CI) (CA INDEX NAME)



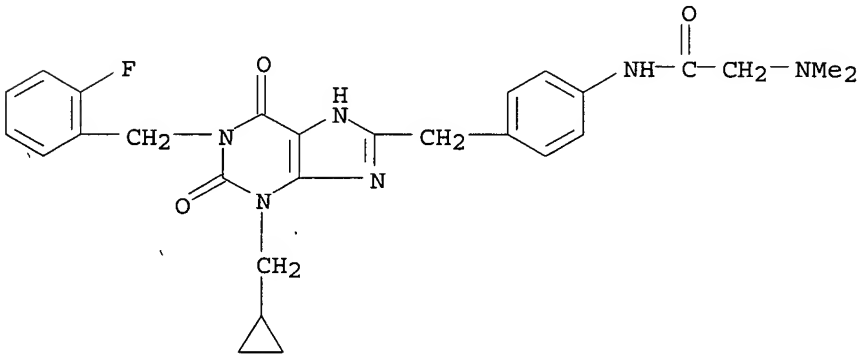
RN 637335-84-3 HCAPLUS
CN 1H-Pyrazole-4-carboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-1-methyl- (9CI) (CA INDEX NAME)



RN 637335-87-6 HCAPLUS
CN Acetamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-2-(dimethylamino)-, trifluoroacetate (9CI) (CA INDEX NAME)

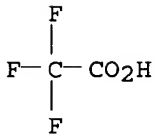
CM 1

CRN 637335-86-5
CMF C27 H29 F N6 O3

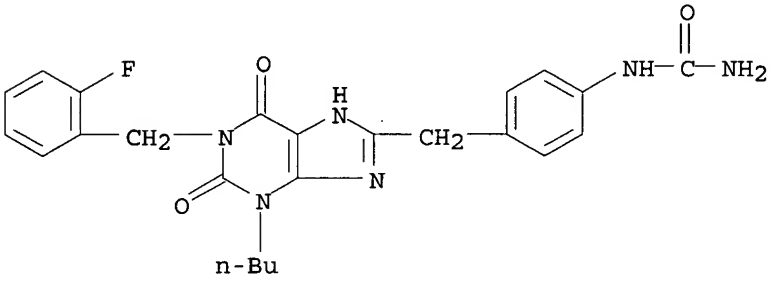


CM 2

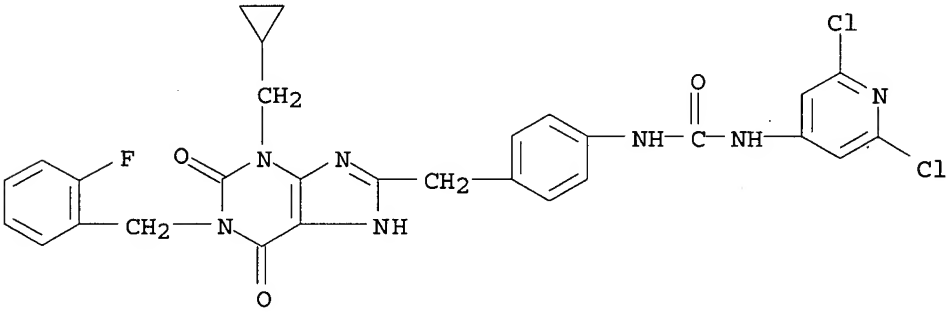
CRN 76-05-1
CMF C2 H F3 O2



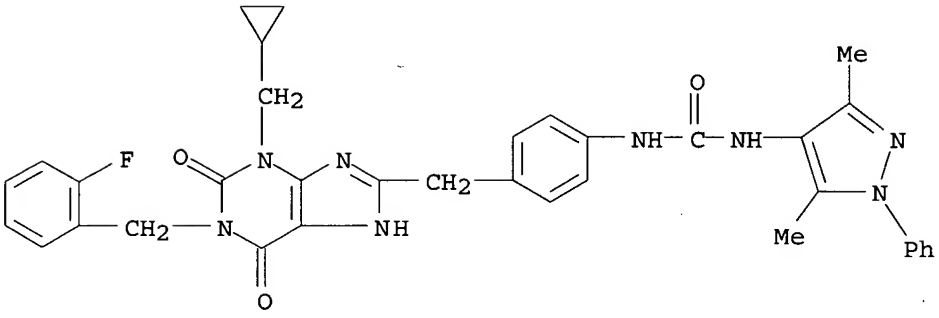
RN 637335-88-7 HCAPLUS
CN Urea, [4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 637335-91-2 HCAPLUS
CN Urea, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N'-(2,6-dichloro-4-pyridinyl)- (9CI) (CA INDEX NAME)

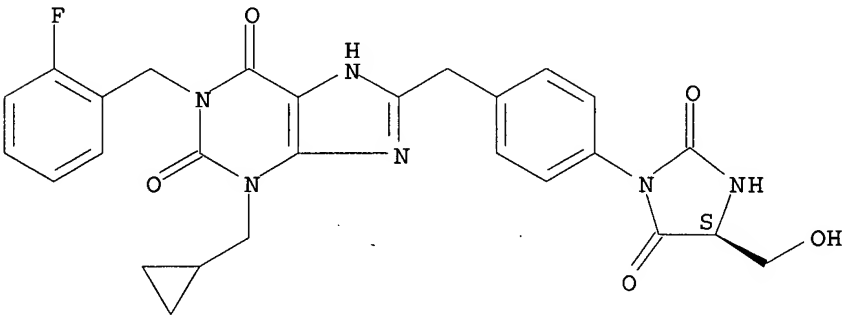


RN 637335-92-3 HCAPLUS
CN Urea, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N'-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)

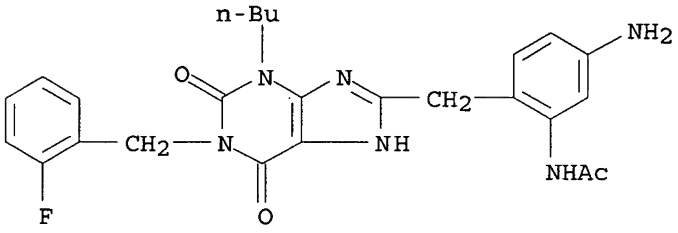


RN 637335-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-3,7-dihydro-8-[[4-[(4S)-4-(hydroxymethyl)-2,5-dioxo-1-imidazolidinyl]phenyl]methyl]- (9CI) (CA INDEX NAME)

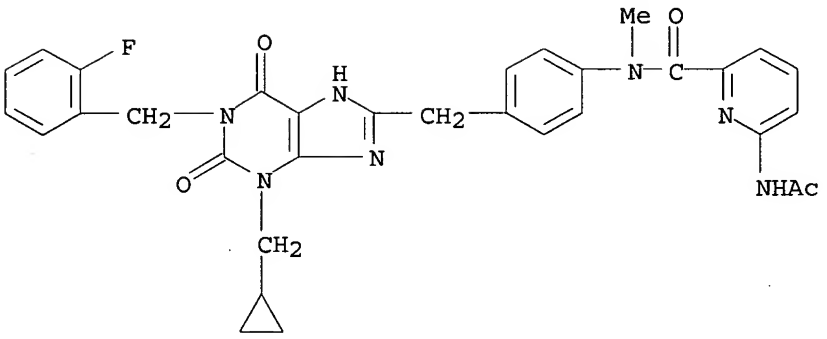
Absolute stereochemistry.



RN 637335-99-0 HCAPLUS
CN Acetamide, N-[5-amino-2-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



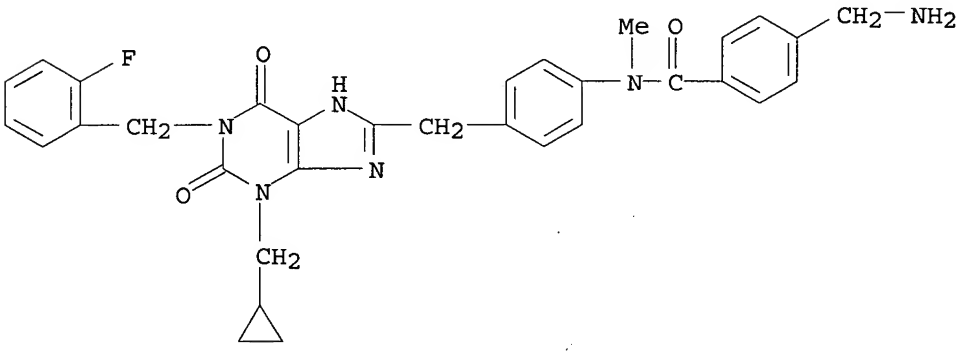
RN 637336-00-6 HCAPLUS
CN 2-Pyridinecarboxamide, 6-(acetylamino)-N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N-methyl- (9CI) (CA INDEX NAME)



RN 637336-04-0 HCAPLUS
CN Benzamide, 4-(aminomethyl)-N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N-methyl-, trifluoroacetate (9CI) (CA INDEX NAME)

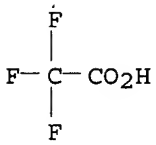
CM 1

CRN 637336-03-9
CMF C32 H31 F N6 O3



CM 2

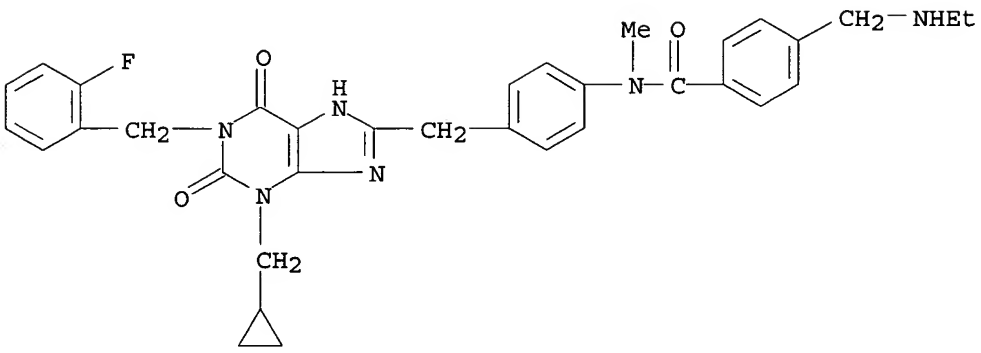
CRN 76-05-1
CMF C2 H F3 O2



RN 637336-06-2 HCAPLUS
CN Benzamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-4-[(ethylamino)methyl]-N-methyl-, trifluoroacetate (9CI) (CA INDEX NAME)

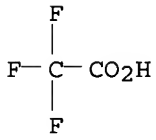
CM 1

CRN 637336-05-1
CMF C34 H35 F N6 O3

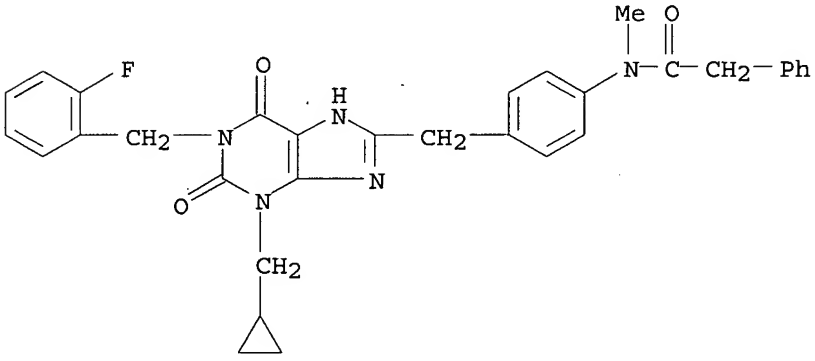


CM 2

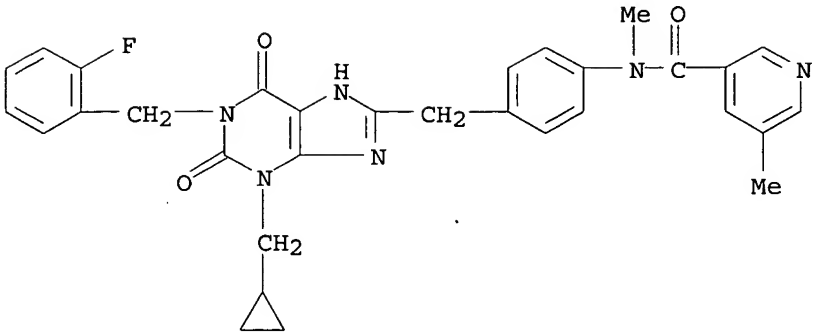
CRN 76-05-1
CMF C2 H F3 O2



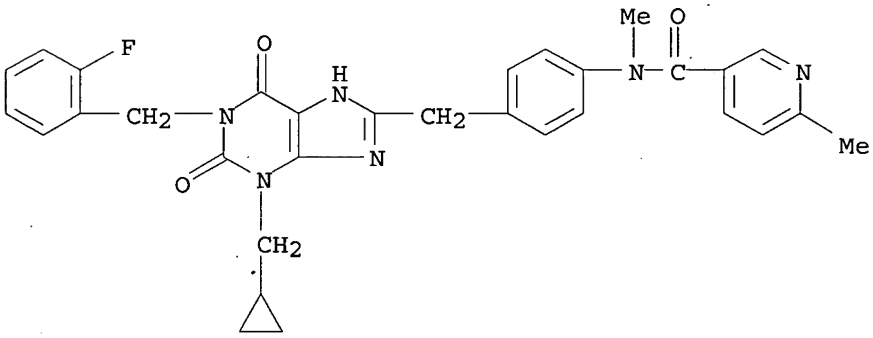
RN 637336-08-4 HCAPLUS
CN Benzeneacetamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N-methyl- (9CI) (CA INDEX NAME)



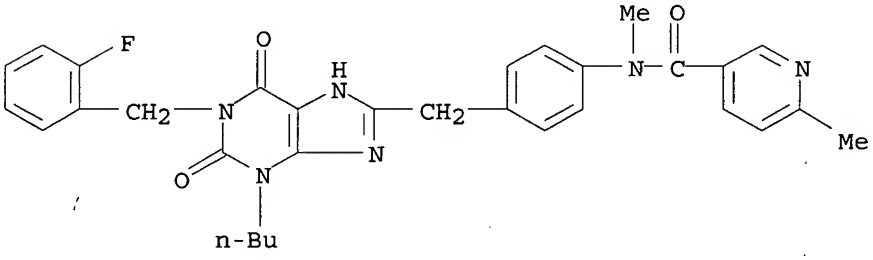
RN 637336-09-5 HCAPLUS
CN 3-Pyridinecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,5-dimethyl- (9CI) (CA INDEX NAME)



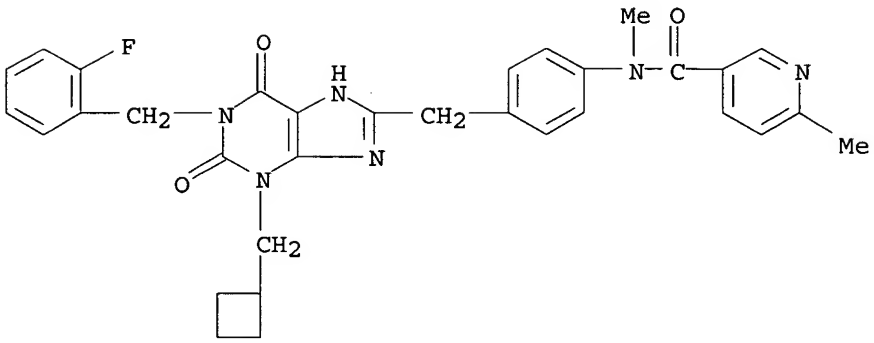
RN 637336-10-8 HCAPLUS
CN 3-Pyridinecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,6-dimethyl- (9CI) (CA INDEX NAME)



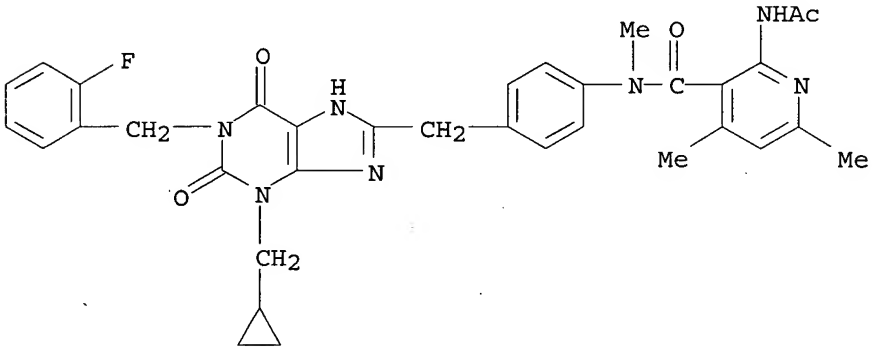
RN 637336-11-9 HCAPLUS
CN 3-Pyridinecarboxamide, N-[4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,6-dimethyl- (9CI) (CA INDEX NAME)



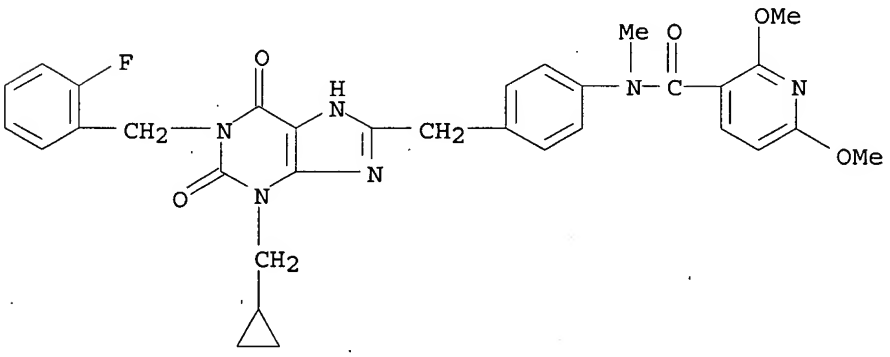
RN 637336-14-2 HCAPLUS
CN 3-Pyridinecarboxamide, N-[4-[[3-(cyclobutylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,6-dimethyl- (9CI) (CA INDEX NAME)



RN 637336-18-6 HCAPLUS
CN 3-Pyridinecarboxamide, 2-(acetylamino)-N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,4,6-trimethyl- (9CI) (CA INDEX NAME)

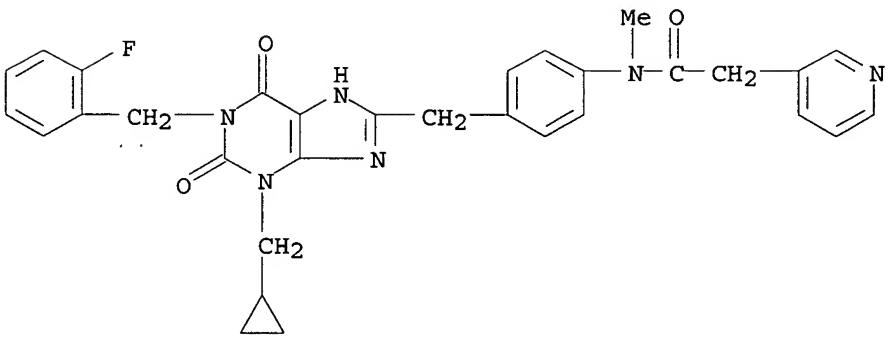


RN 637336-19-7 HCAPLUS
CN 3-Pyridinecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-2,6-dimethoxy-N-methyl- (9CI) (CA INDEX NAME)

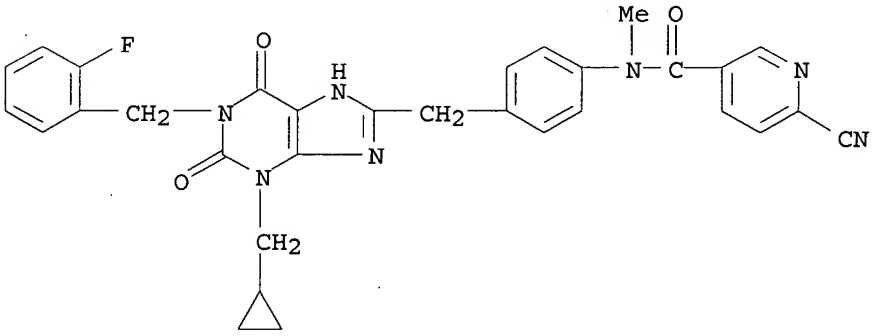


RN 637336-20-0 HCAPLUS
CN 3-Pyridineacetamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-

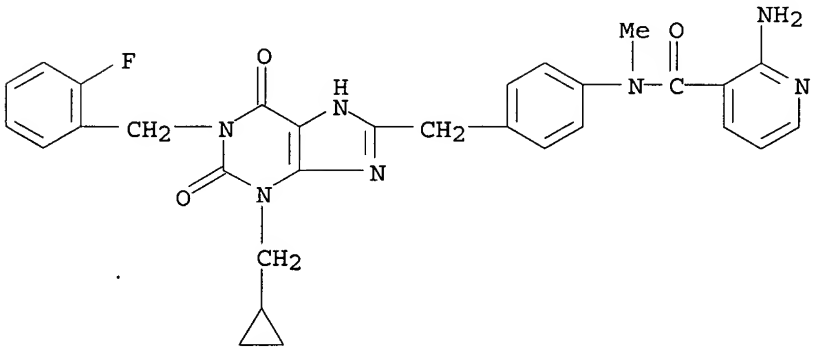
yl]methyl]phenyl]-N-methyl- (9CI) (CA INDEX NAME)



RN 637336-21-1 HCAPLUS
CN 3-Pyridinecarboxamide, 6-cyano-N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N-methyl- (9CI) (CA INDEX NAME)

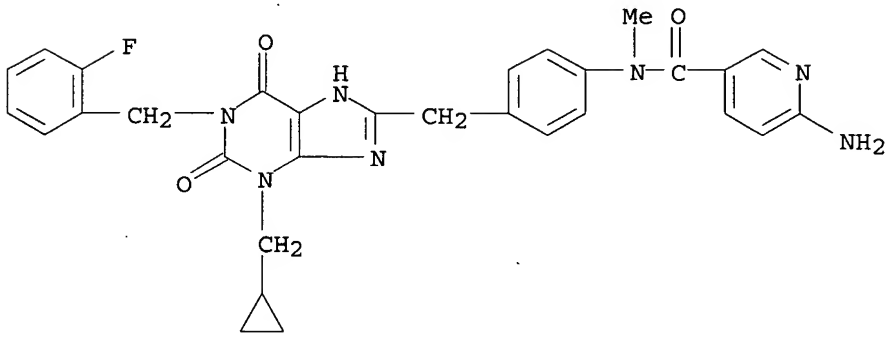


RN 637336-22-2 HCAPLUS
CN 3-Pyridinecarboxamide, 2-amino-N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N-methyl- (9CI) (CA INDEX NAME)

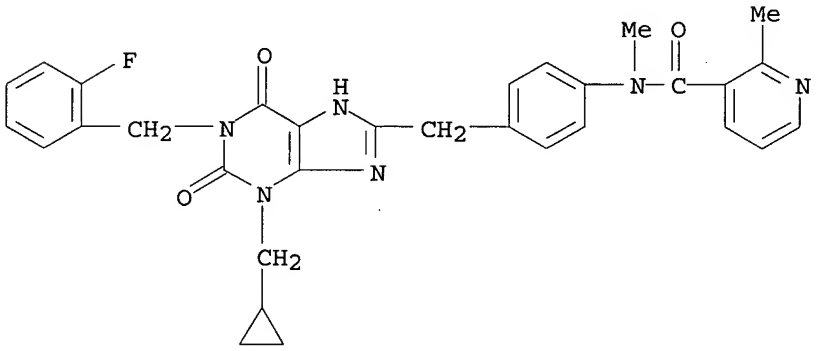


RN 637336-23-3 HCAPLUS
CN 3-Pyridinecarboxamide, 6-amino-N-[4-[[3-(cyclopropylmethyl)-1-[(2-

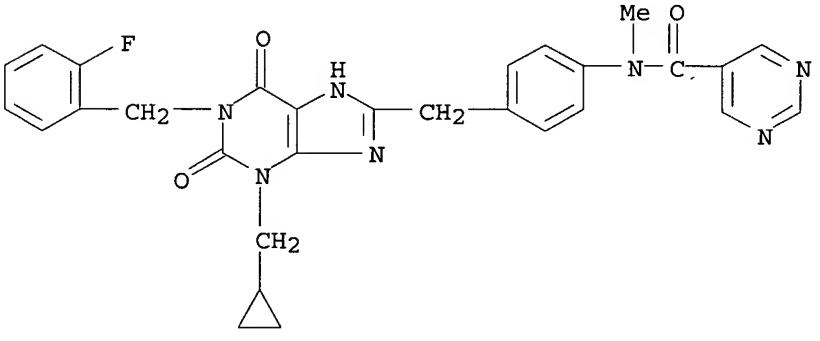
fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N-methyl- (9CI) (CA INDEX NAME)



RN 637336-25-5 HCAPLUS
CN 3-Pyridinecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,2-dimethyl- (9CI) (CA INDEX NAME)

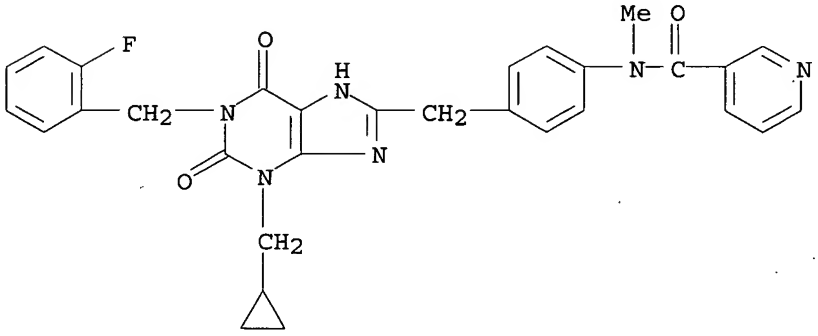


RN 637336-26-6 HCAPLUS
CN 5-Pyrimidinecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N-methyl- (9CI) (CA INDEX NAME)

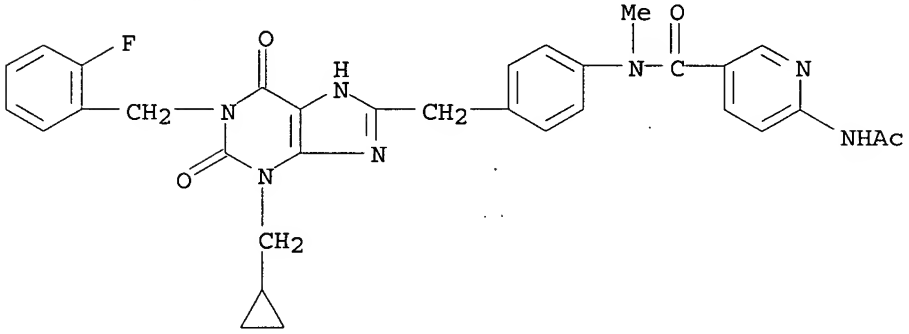


RN 637336-27-7 HCAPLUS

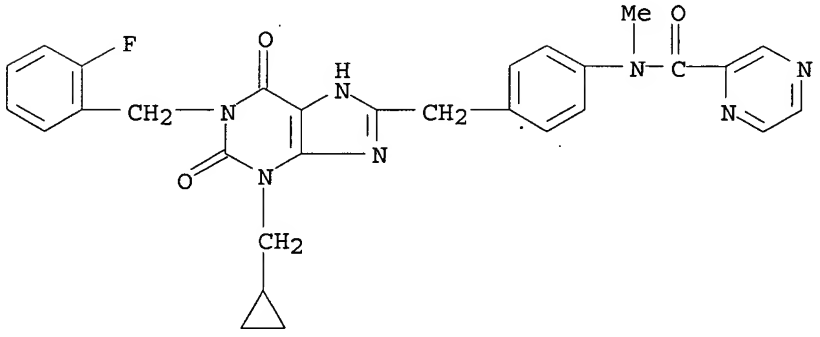
CN 3-Pyridinecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N-methyl- (9CI) (CA INDEX NAME)



RN 637336-28-8 HCAPLUS
CN 3-Pyridinecarboxamide, 6-(acetylamino)-N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N-methyl- (9CI) (CA INDEX NAME)

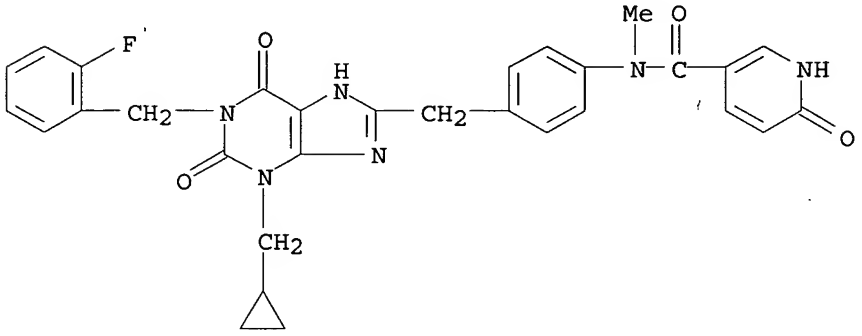


RN 637336-29-9 HCAPLUS
CN Pyrazinecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N-methyl- (9CI) (CA INDEX NAME)

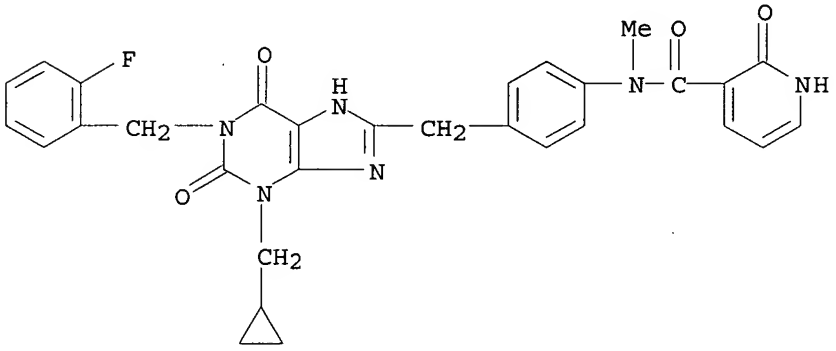


RN 637336-30-2 HCAPLUS

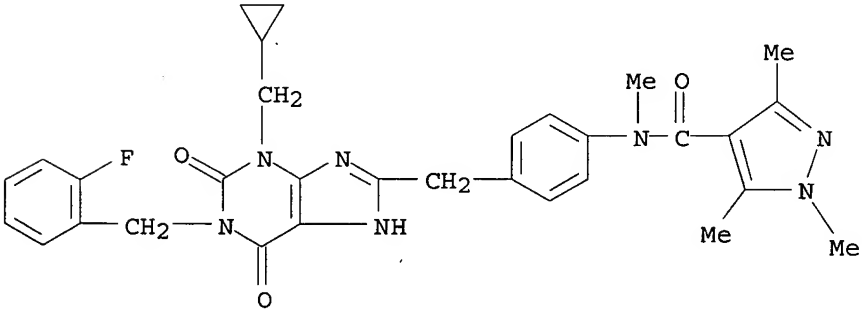
CN 3-Pyridinecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-1,6-dihydro-N-methyl-6-oxo- (9CI) (CA INDEX NAME)



RN 637336-31-3 HCAPLUS
CN 3-Pyridinecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-1,2-dihydro-N-methyl-2-oxo- (9CI) (CA INDEX NAME)

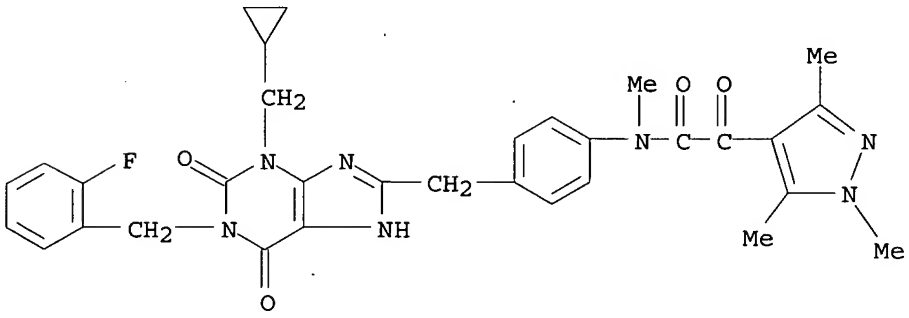


RN 637336-32-4 HCAPLUS
CN 1H-Pyrazole-4-carboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,1,3,5-tetramethyl- (9CI) (CA INDEX NAME)

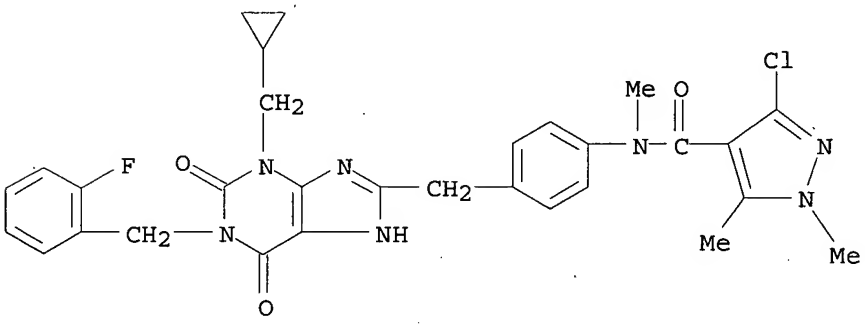


RN 637336-33-5 HCAPLUS

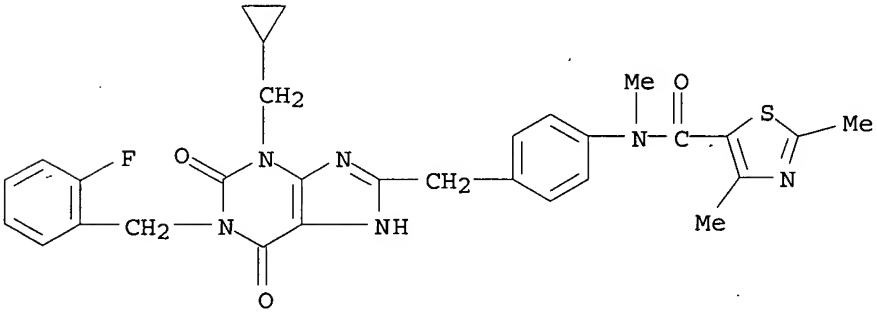
CN 1H-Pyrazole-4-acetamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,1,3,5-tetramethyl-α-oxo- (9CI) (CA INDEX NAME)



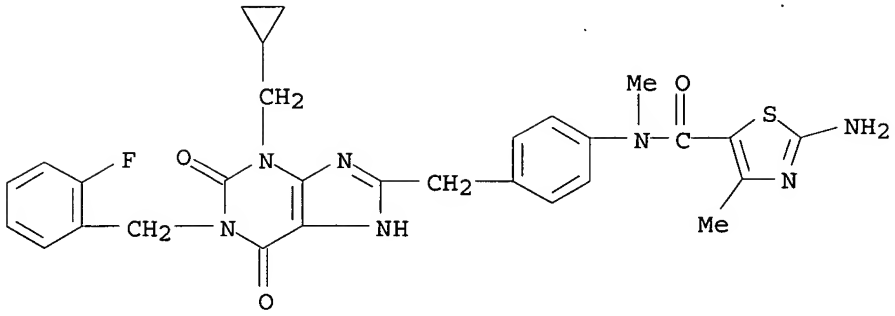
RN 637336-35-7 HCAPLUS
CN 1H-Pyrazole-4-carboxamide, 3-chloro-N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,1,5-trimethyl- (9CI) (CA INDEX NAME)



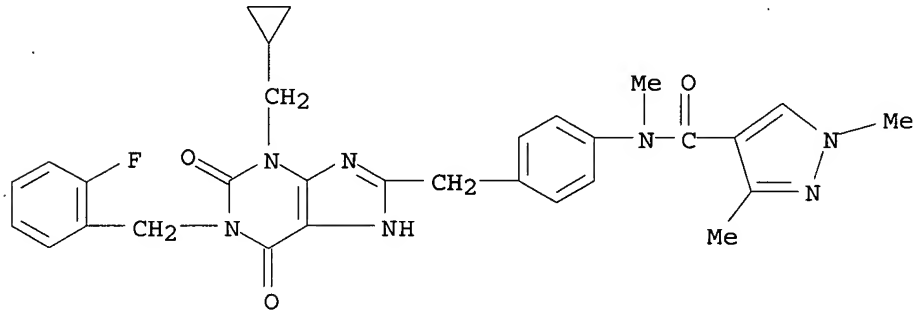
RN 637336-36-8 HCAPLUS
CN 5-Thiazolecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,2,4-trimethyl- (9CI) (CA INDEX NAME)



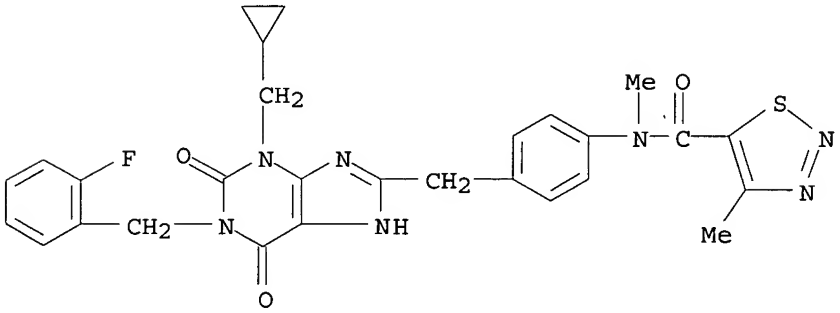
RN 637336-37-9 HCAPLUS
CN 5-Thiazolecarboxamide, 2-amino-N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,4-dimethyl- (9CI) (CA INDEX NAME)



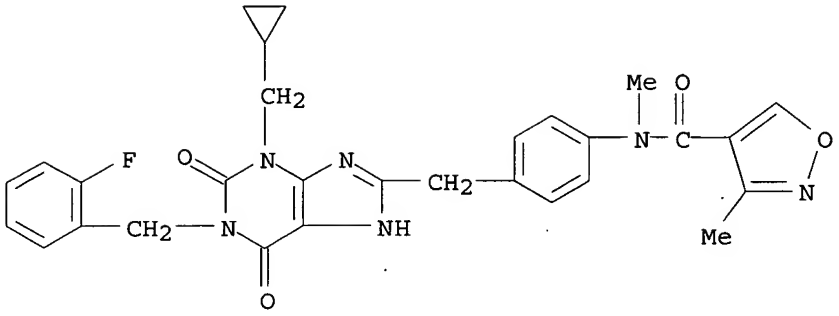
RN 637336-40-4 HCAPLUS
CN 1H-Pyrazole-4-carboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,1,3-trimethyl- (9CI) (CA INDEX NAME)



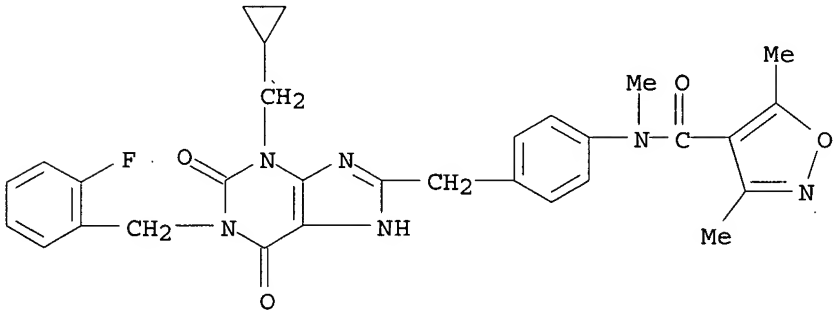
RN 637336-42-6 HCAPLUS
CN 1,2,3-Thiadiazole-5-carboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,4-dimethyl- (9CI) (CA INDEX NAME)



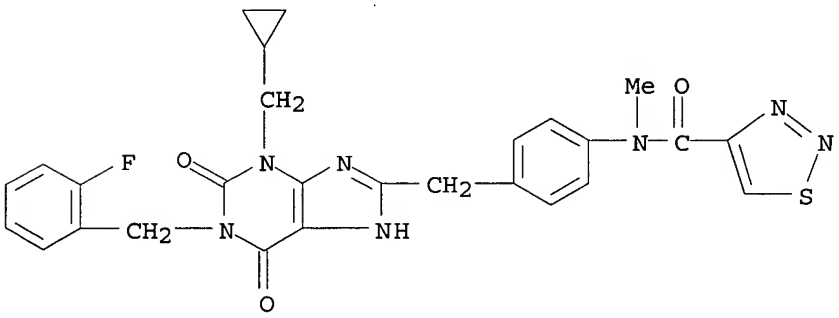
RN 637336-43-7 HCAPLUS
CN 4-Isoxazolecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)



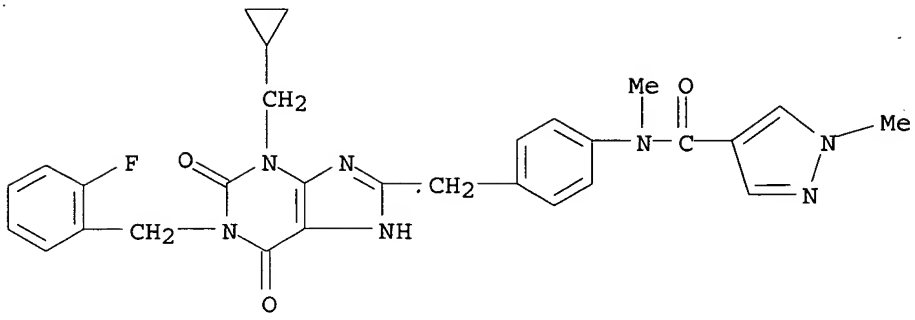
RN 637336-44-8 HCAPLUS
CN 4-Isoxazolecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,3,5-trimethyl- (9CI) (CA INDEX NAME)



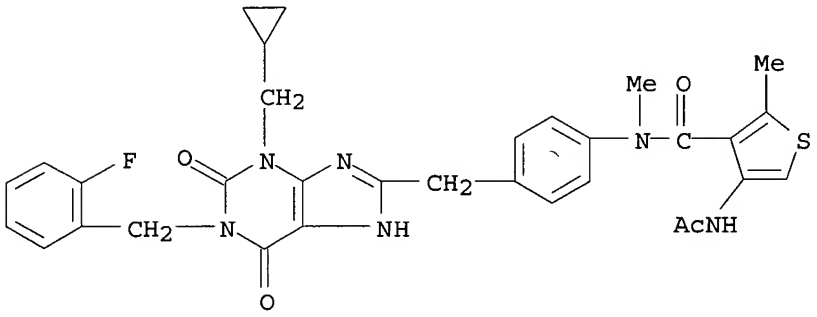
RN 637336-45-9 HCAPLUS
CN 1,2,3-Thiadiazole-4-carboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N-methyl- (9CI) (CA INDEX NAME)



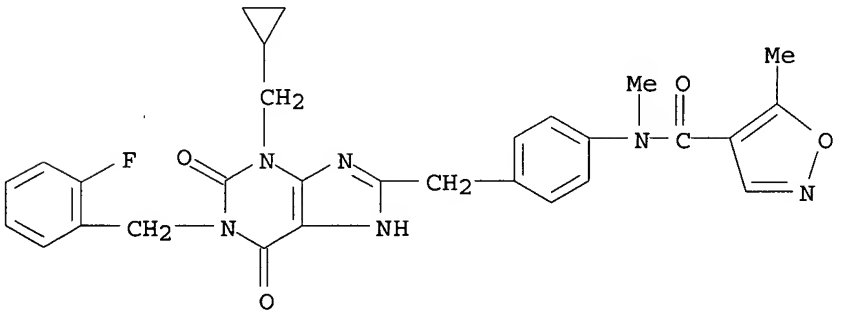
RN 637336-46-0 HCAPLUS
CN 1H-Pyrazole-4-carboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,1-dimethyl- (9CI) (CA INDEX NAME)



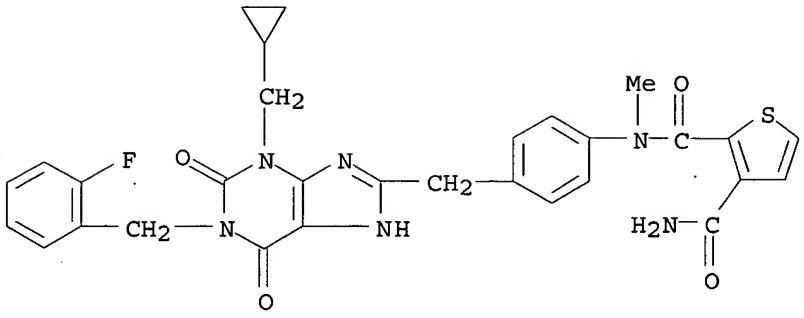
RN 637336-47-1 HCAPLUS
CN 3-Thiophenecarboxamide, 4-(acetylamino)-N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,2-dimethyl- (9CI) (CA INDEX NAME)



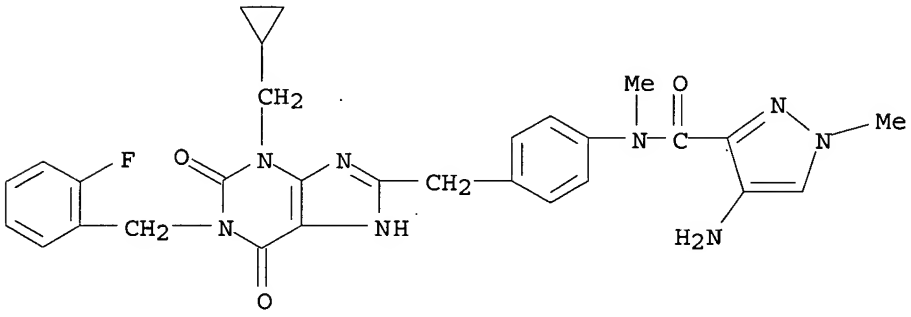
RN 637336-49-3 HCAPLUS
CN 4-Isoxazolecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,5-dimethyl- (9CI) (CA INDEX NAME)



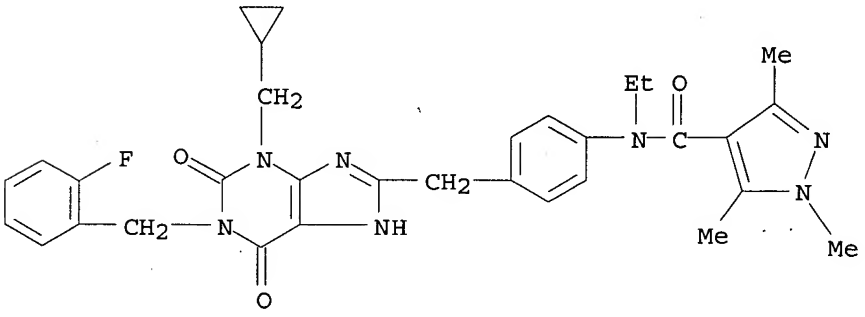
RN 637336-50-6 HCAPLUS
CN 2,3-Thiophenedicarboxamide, N2-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N2-methyl- (9CI) (CA INDEX NAME)



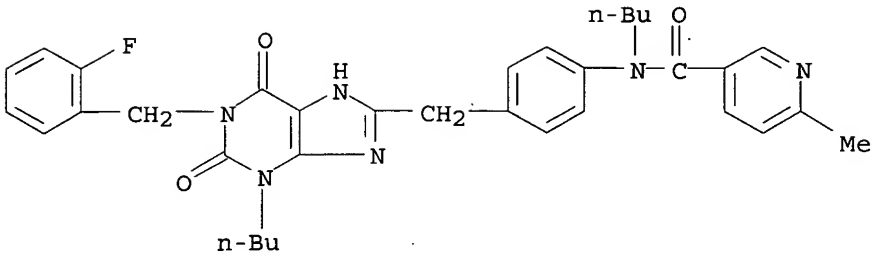
RN 637336-52-8 HCAPLUS
CN 1H-Pyrazole-3-carboxamide, 4-amino-N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,1-dimethyl- (9CI) (CA INDEX NAME)



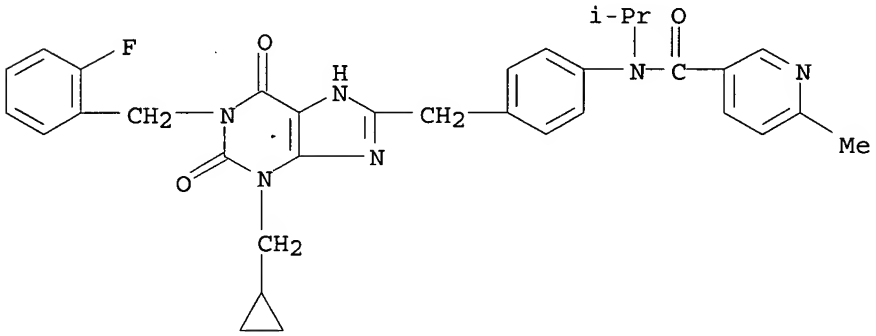
RN 637336-57-3 HCAPLUS
CN 1H-Pyrazole-4-carboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N-ethyl-1,3,5-trimethyl- (9CI) (CA INDEX NAME)



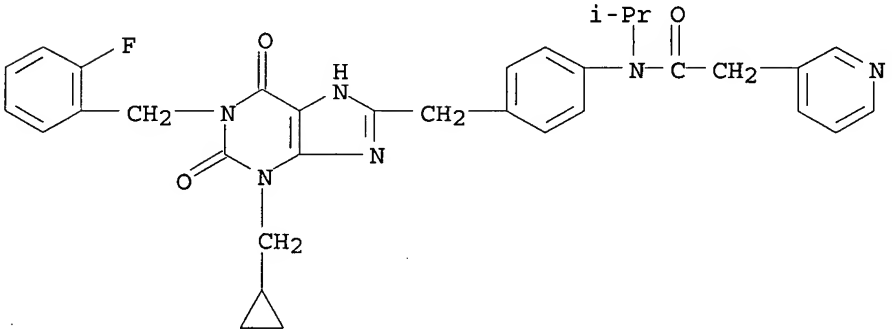
RN 637336-59-5 HCAPLUS
CN 3-Pyridinecarboxamide, N-butyl-N-[4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-6-methyl- (9CI) (CA INDEX NAME)



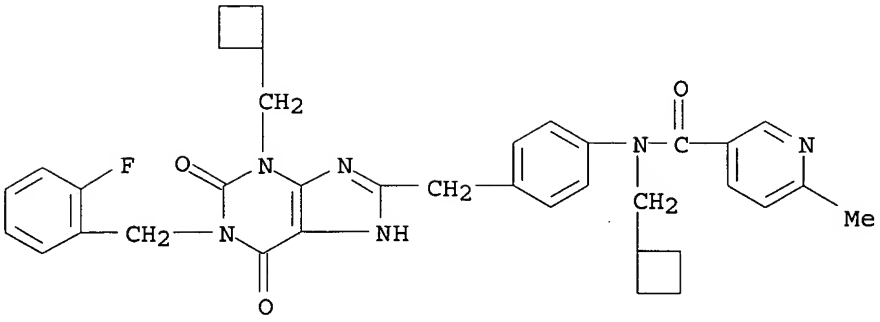
RN 637336-60-8 HCAPLUS
CN 3-Pyridinecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-6-methyl-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



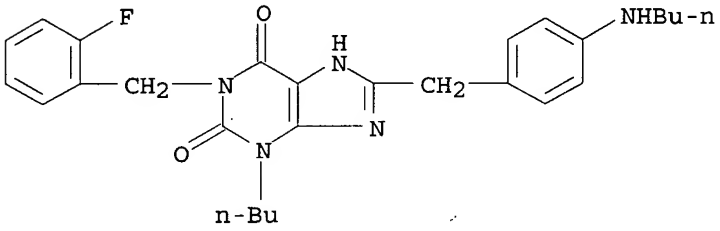
RN 637336-62-0 HCAPLUS
CN 3-Pyridineacetamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



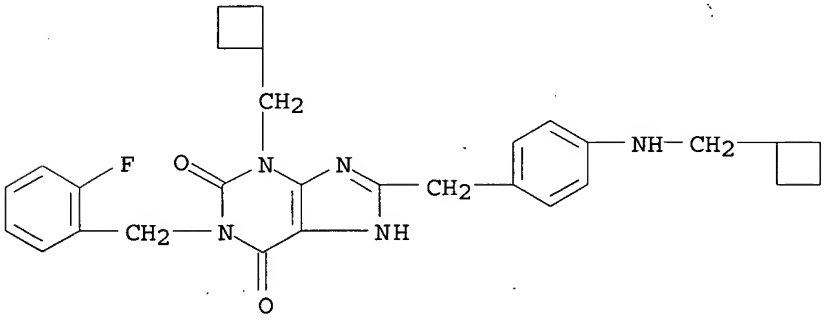
RN 637336-63-1 HCAPLUS
CN 3-Pyridinecarboxamide, N-(cyclobutylmethyl)-N-[4-[[3-(cyclobutylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-6-methyl- (9CI) (CA INDEX NAME)



IT **637336-12-0P 637336-16-4P**
RL: BYP (Byproduct); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amide-substituted xanthine derivs. as phosphoenolpyruvate carboxykinase inhibitors with gluconeogenesis modulating activity for treating type 2 diabetes)
RN 637336-12-0 HCAPLUS
CN 1H-Purine-2,6-dione, 3-butyl-8-[[4-(butylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-3,7-dihydro- (9CI) (CA INDEX NAME)

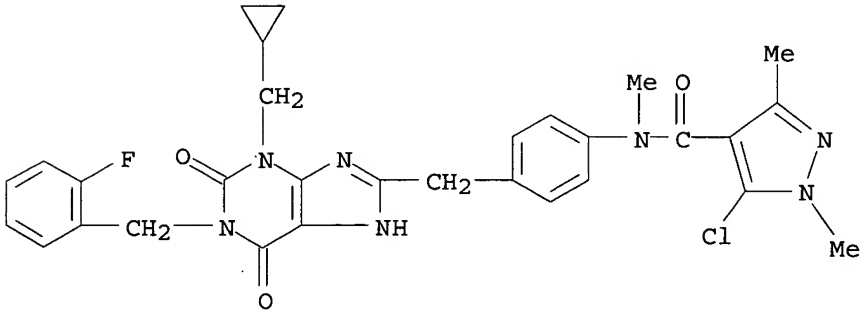


RN 637336-16-4 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclobutylmethyl)-8-[[4-[(cyclobutylmethyl)amino]phenyl]methyl]-1-[(2-fluorophenyl)methyl]-3,7-dihydro- (9CI) (CA INDEX NAME)



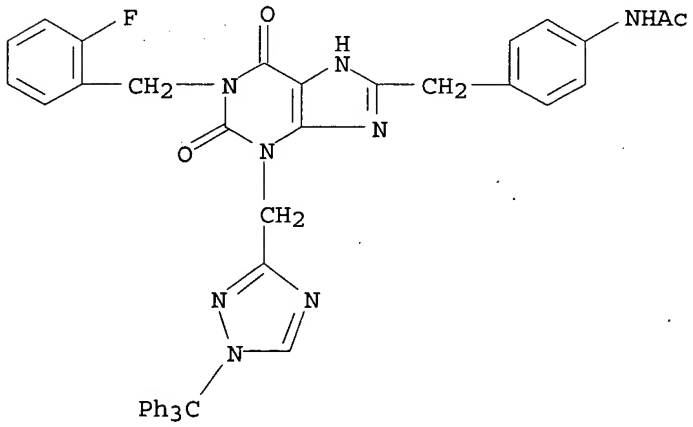
IT **637336-41-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amide-substituted xanthine derivs. as phosphoenolpyruvate carboxykinase inhibitors with gluconeogenesis modulating activity for treating type 2 diabetes)
RN 637336-41-5 HCAPLUS

CN 1H-Pyrazole-4-carboxamide, 5-chloro-N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,1,3-trimethyl- (9CI) (CA INDEX NAME)

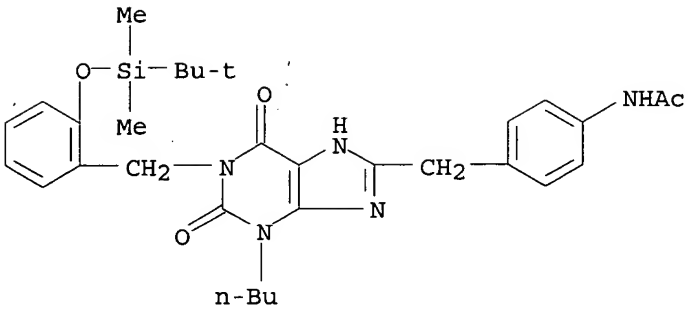


IT **637335-12-7P 637335-67-2P 637335-70-7P**
637335-76-3P 637335-80-9P 637335-82-1P
637335-85-4P 637335-90-1P 637336-01-7P
637336-13-1P 637336-15-3P 637336-17-5P
637336-24-4P 637336-39-1P 637336-58-4P
637336-61-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amide-substituted xanthine derivs. as phosphoenolpyruvate carboxykinase inhibitors with gluconeogenesis modulating activity for treating type 2 diabetes)

RN 637335-12-7 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-3-[[1-(triphenylmethyl)-1H-1,2,4-triazol-3-yl]methyl]-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)

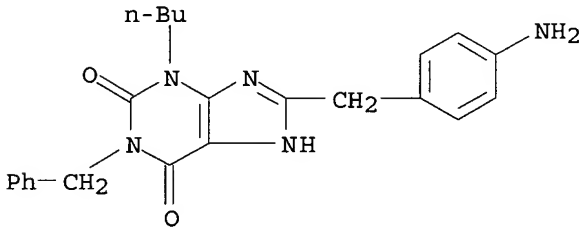


RN 637335-67-2 HCAPLUS
CN Acetamide, N-[4-[[3-butyl-1-[[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]phenyl]methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-, monosodium salt (9CI) (CA INDEX NAME)

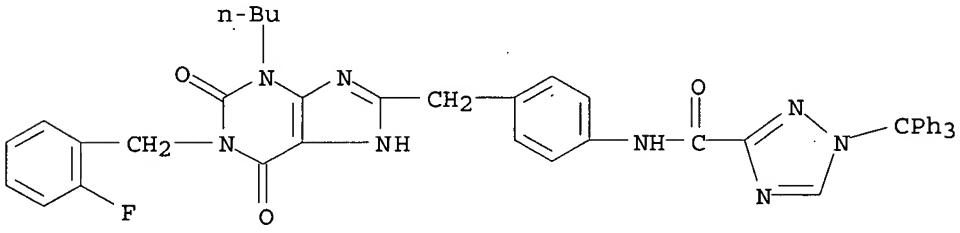


● Na

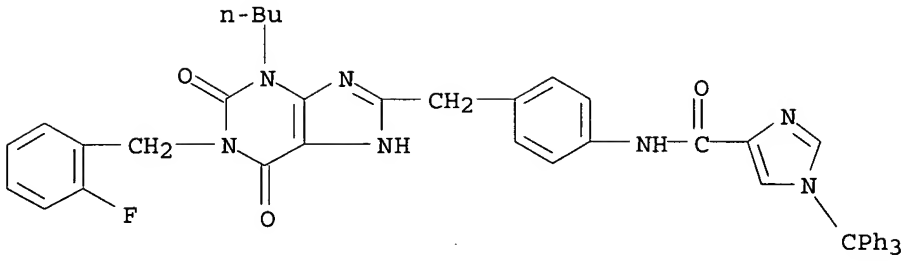
RN 637335-70-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(4-aminophenyl)methyl]-3-butyl-3,7-dihydro-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



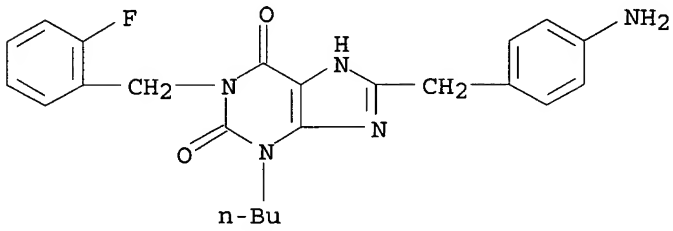
RN 637335-76-3 HCAPLUS
CN 1H-1,2,4-Triazole-3-carboxamide, N-[4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-1-(triphenylmethyl)- (9CI) (CA INDEX NAME)



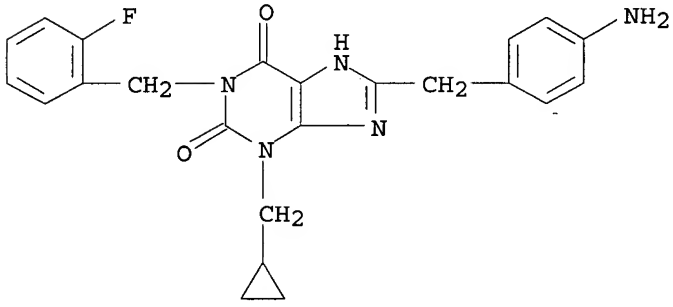
RN 637335-80-9 HCAPLUS
CN 1H-Imidazole-4-carboxamide, N-[4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-1-(triphenylmethyl)- (9CI) (CA INDEX NAME)



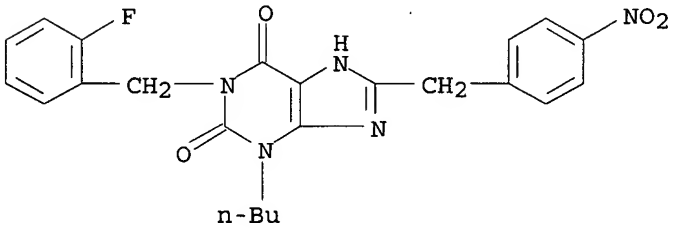
RN 637335-82-1 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(4-aminophenyl)methyl]-3-butyl-1-[(2-fluorophenyl)methyl]-3,7-dihydro- (9CI) (CA INDEX NAME)



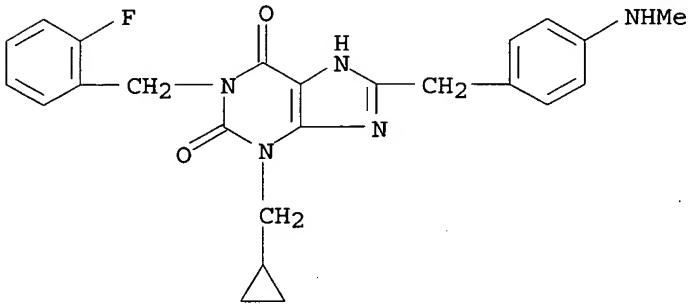
RN 637335-85-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(4-aminophenyl)methyl]-3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-3,7-dihydro- (9CI) (CA INDEX NAME)



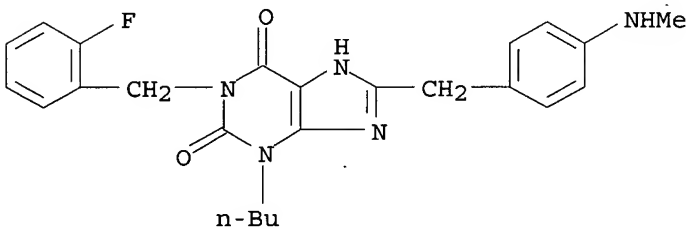
RN 637335-90-1 HCAPLUS
CN 1H-Purine-2,6-dione, 3-butyl-1-[(2-fluorophenyl)methyl]-3,7-dihydro-8-[(4-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)



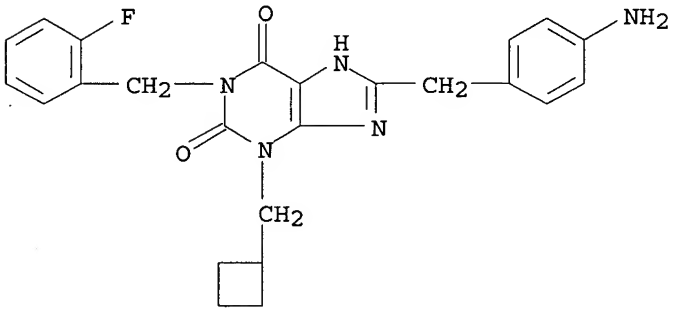
RN 637336-01-7 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-3,7-dihydro-8-[[4-(methylamino)phenyl]methyl]- (9CI) (CA INDEX NAME)



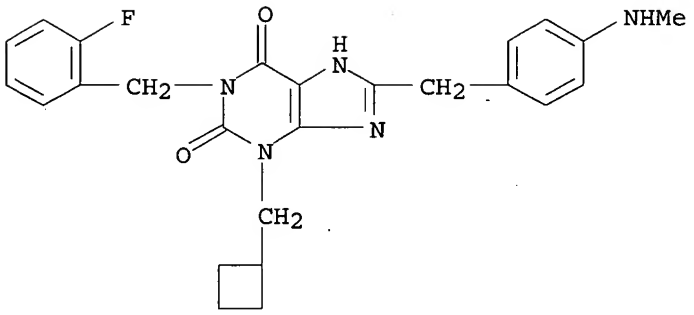
RN 637336-13-1 HCAPLUS
CN 1H-Purine-2,6-dione, 3-butyl-1-[(2-fluorophenyl)methyl]-3,7-dihydro-8-[[4-(methylamino)phenyl]methyl]- (9CI) (CA INDEX NAME)



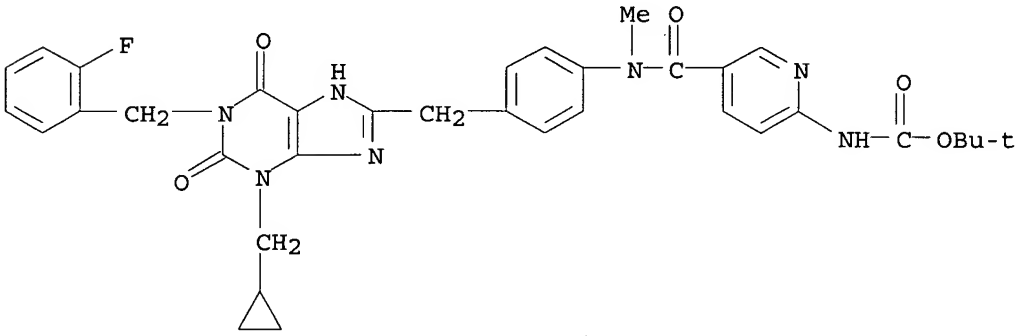
RN 637336-15-3 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(4-aminophenyl)methyl]-3-(cyclobutylmethyl)-1-[(2-fluorophenyl)methyl]-3,7-dihydro- (9CI) (CA INDEX NAME)



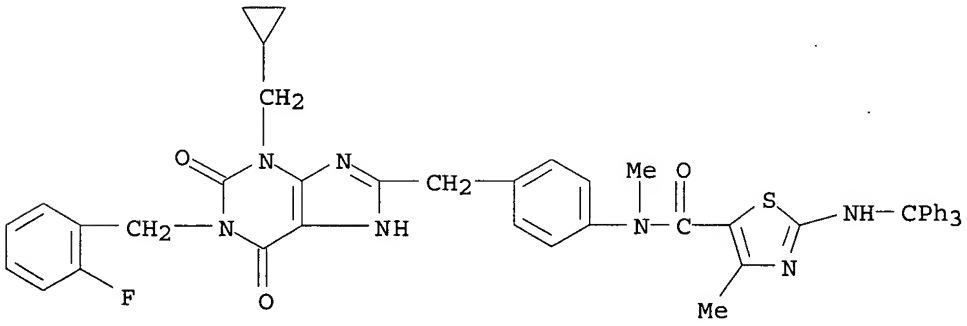
RN 637336-17-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclobutylmethyl)-1-[(2-fluorophenyl)methyl]-3,7-dihydro-8-[[4-(methylamino)phenyl]methyl]- (9CI) (CA INDEX NAME)



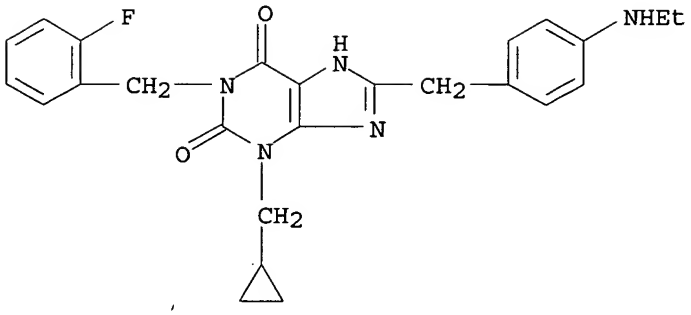
RN 637336-24-4 HCAPLUS
CN Carbamic acid, [5-[[[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]methylamino]carbonyl]-2-pyridinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



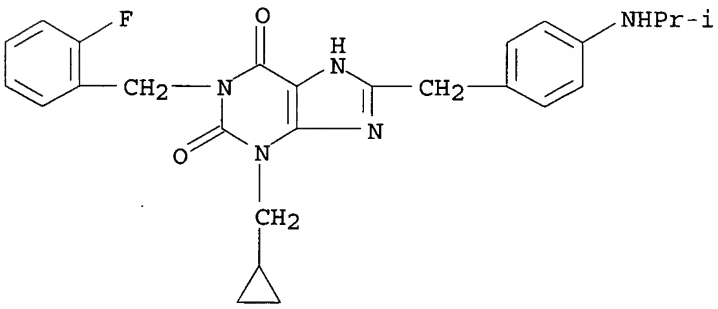
RN 637336-39-1 HCAPLUS
CN 5-Thiazolecarboxamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-N,4-dimethyl-2-[(triphenylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 637336-58-4 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclopropylmethyl)-8-[[4-(ethylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-3,7-dihydro- (9CI) (CA INDEX NAME)

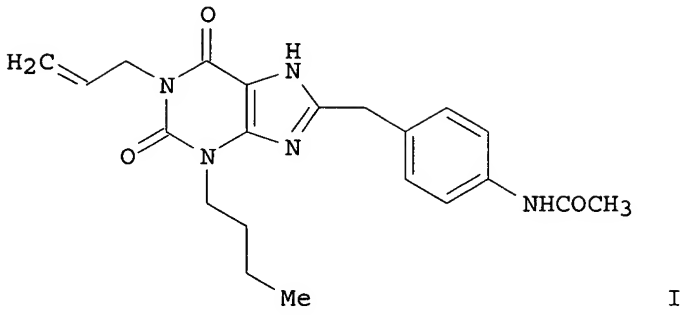


RN 637336-61-9 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-3,7-dihydro-8-[[4-[(1-methylethyl)amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:795126 HCAPLUS
DOCUMENT NUMBER: 140:70298
TITLE: X-ray structures of two xanthine inhibitors bound to PEPCK and N-3 modifications of substituted 1,8-dibenzylxanthines
AUTHOR(S): Foley, Louise H.; Wang, Ping; Dunten, Pete; Ramsey, Gwendolyn; Gubler, Mary-Lou; Wertheimer, Stanley J.
CORPORATE SOURCE: Department of Discovery Chemistry, Roche Research Center, Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(21), 3871-3874
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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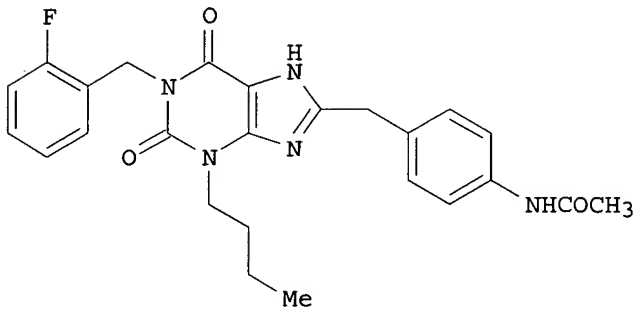


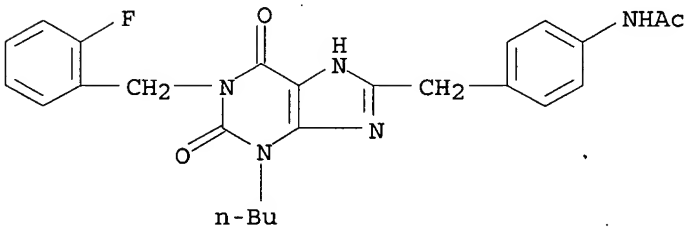
II

AB The anal. of the X-ray structures of two xanthine inhibitors bound to PEPCK and a comparison to the X-ray structure of GTP bound to PEPCK are reported. The SAR at N-1, N-7 and developing SAR at C-8 are consistent with information gained from the X-ray structures of compds. I and II bound to PEPCK. Representative N-3 modifications of compound II that led to the discovery of 3-cyclopropylmethyl and its carboxy analog as optimal N-3 groups are presented.

IT **628279-07-2**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(X-ray structures of two xanthine inhibitors bound to PEPCK and N-3 modifications of substituted 1,8-dibenzylxanthines)

RN 628279-07-2 HCAPLUS

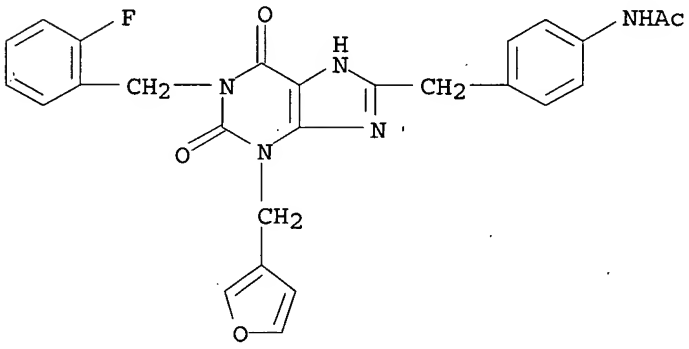
CN Acetamide, N-[4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



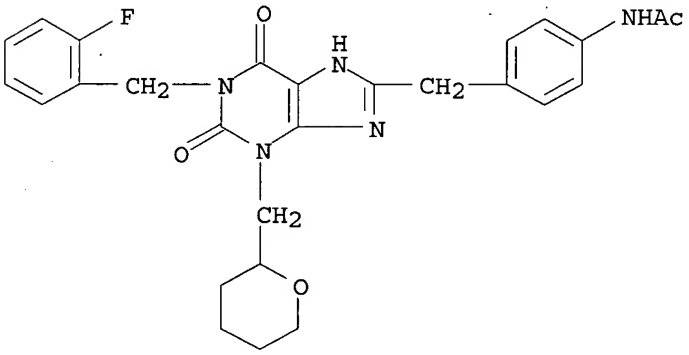
IT **637334-98-6P 637335-05-8P 637335-07-0P**
637335-13-8P 637335-14-9P 637335-17-2P
637335-18-3P 637335-21-8P 637335-28-5P
637335-29-6P 637335-30-9P 637335-36-5P
637335-38-7P 637335-39-8P 637335-45-6P

639780-62-4P 639780-63-5P 639780-64-6P
639780-65-7P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(X-ray structures of two xanthine inhibitors bound to PEPCK and N-3 modifications of substituted 1,8-dibenzylxanthines)

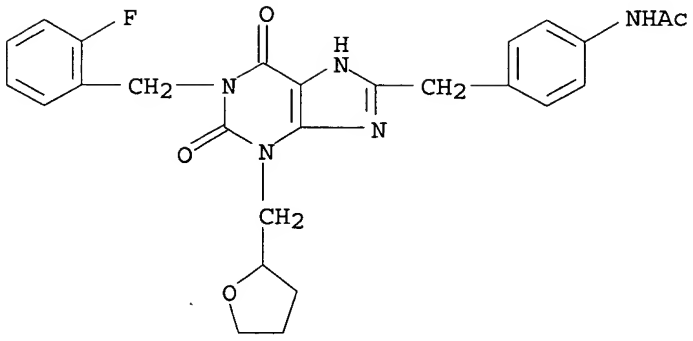
RN 637334-98-6 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-3-(3-furanylmethyl)-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



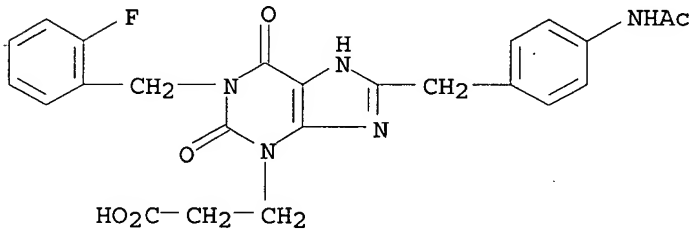
RN 637335-05-8 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-3-[(tetrahydro-2H-pyran-2-yl)methyl]-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



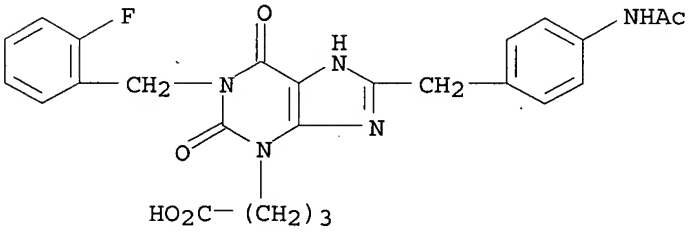
RN 637335-07-0 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-3-[(tetrahydro-2-furanyl)methyl]-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



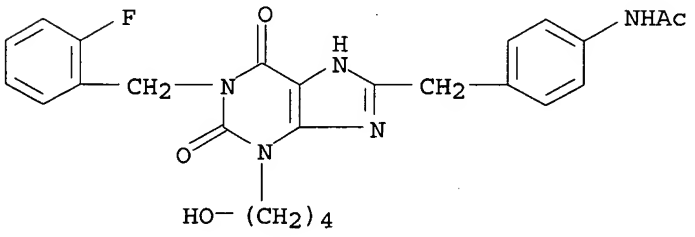
RN 637335-13-8 HCAPLUS
CN 3H-Purine-3-propanoic acid, 8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo- (9CI) (CA INDEX NAME)



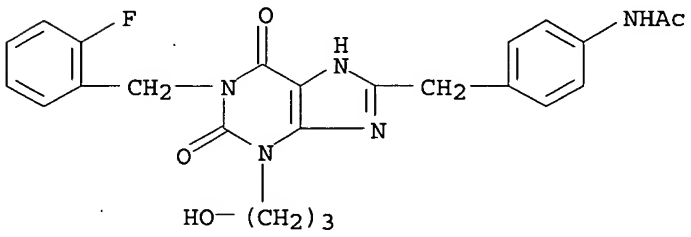
RN 637335-14-9 HCAPLUS
CN 3H-Purine-3-butanoic acid, 8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo- (9CI) (CA INDEX NAME)



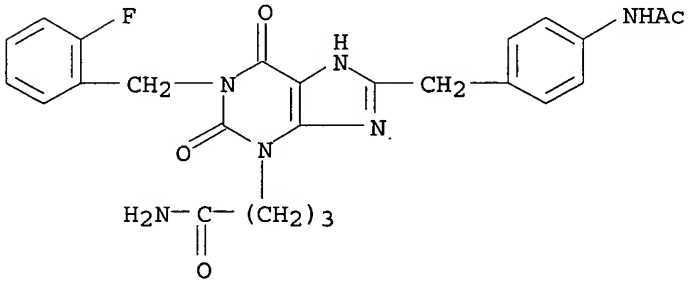
RN 637335-17-2 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-3-(4-hydroxybutyl)-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



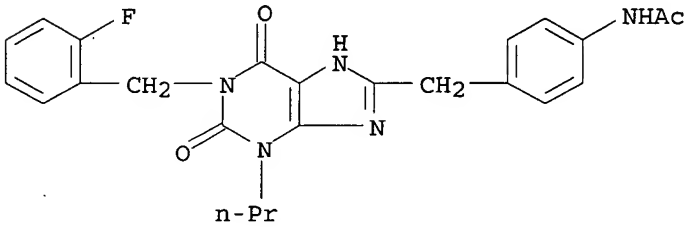
RN 637335-18-3 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-3-(3-hydroxypropyl)-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



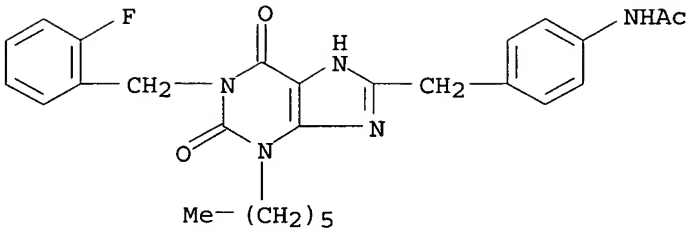
RN 637335-21-8 HCAPLUS
CN 3H-Purine-3-butanamide, 8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo- (9CI) (CA INDEX NAME)



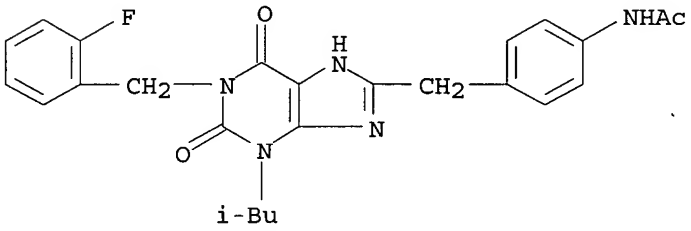
RN 637335-28-5 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-3-propyl-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



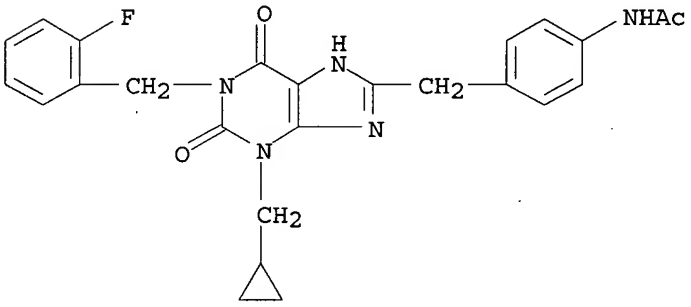
RN 637335-29-6 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-3-hexyl-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



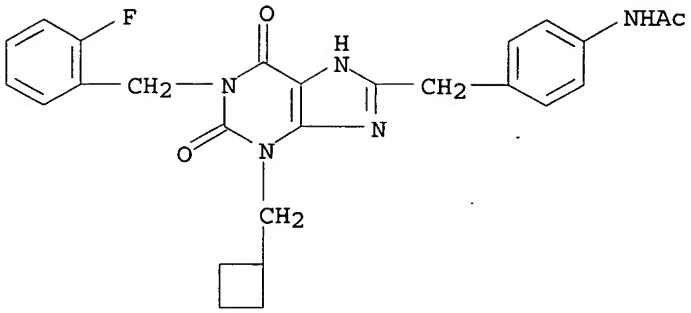
RN 637335-30-9 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-3-(2-methylpropyl)-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



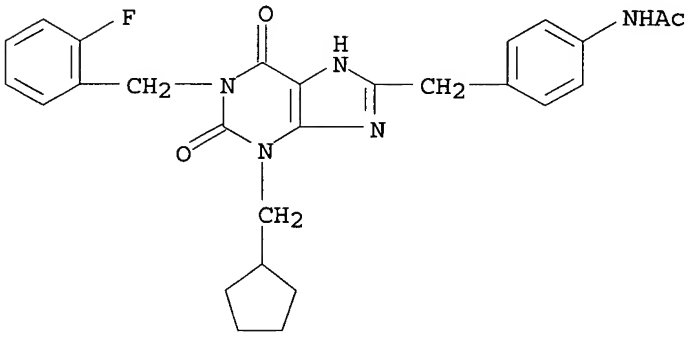
RN 637335-36-5 HCAPLUS
CN Acetamide, N-[4-[[3-(cyclopropylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



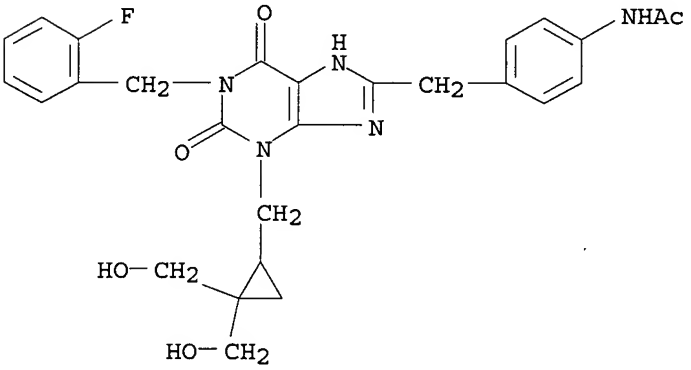
RN 637335-38-7 HCAPLUS
CN Acetamide, N-[4-[[3-(cyclobutylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 637335-39-8 HCAPLUS
CN Acetamide, N-[4-[[3-(cyclopentylmethyl)-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)

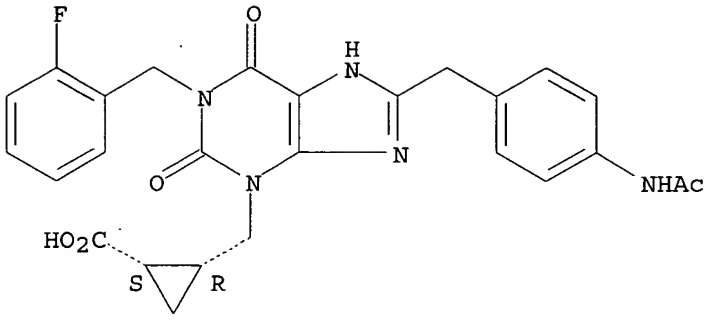


RN 637335-45-6 HCAPLUS
CN Acetamide, N-[4-[[3-[[2,2-bis(hydroxymethyl)cyclopropyl]methyl]-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



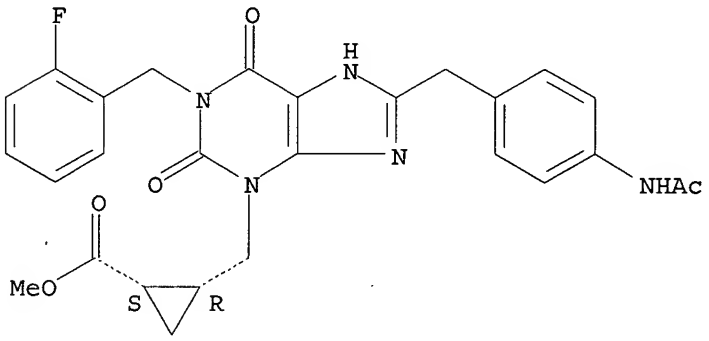
RN 639780-62-4 HCAPLUS
CN Cyclopropanecarboxylic acid, 2-[[8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo-3H-purin-3-yl]methyl]-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



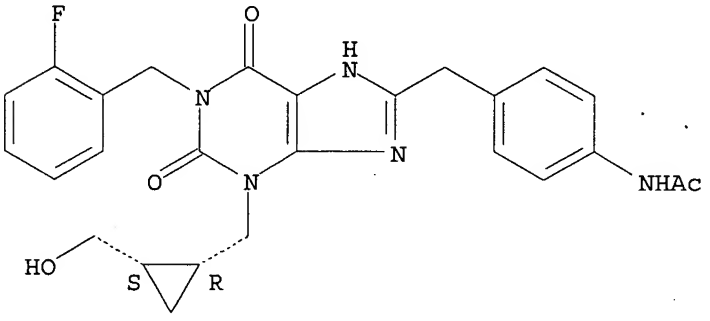
RN 639780-63-5 HCAPLUS
CN Cyclopropanecarboxylic acid, 2-[[8-[[4-(acetylamino)phenyl]methyl]-1-[(2-fluorophenyl)methyl]-1,2,6,7-tetrahydro-2,6-dioxo-3H-purin-3-yl]methyl]-, methyl ester, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



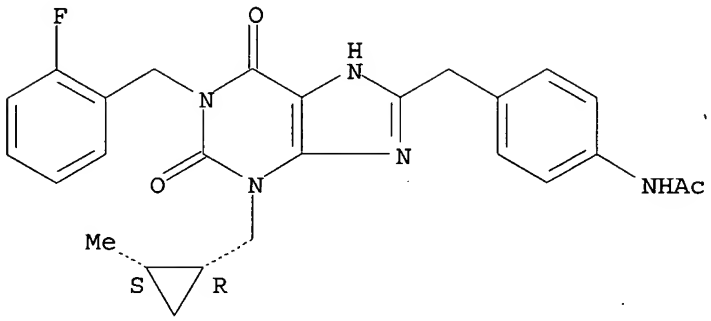
RN 639780-64-6 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-3-[[(1R,2S)-2-(hydroxymethyl)cyclopropyl]methyl]-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 639780-65-7 HCAPLUS
CN Acetamide, N-[4-[[1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-3-[[(1R,2S)-2-methylcyclopropyl]methyl]-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



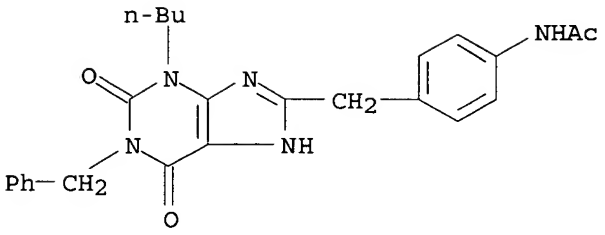
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:746361 HCAPLUS
DOCUMENT NUMBER: 140:229
TITLE: Modified 3-alkyl-1,8-dibenzylxanthines as GTP-competitive inhibitors of phosphoenolpyruvate carboxykinase
AUTHOR(S): Foley, Louise H.; Wang, Ping; Dunten, Pete; Ramsey, Gwendolyn; Gubler, Mary-Lou; Wertheimer, Stanley J.
CORPORATE SOURCE: Roche Research Center, Department of Discovery Chemistry, Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(20), 3607-3610
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:229

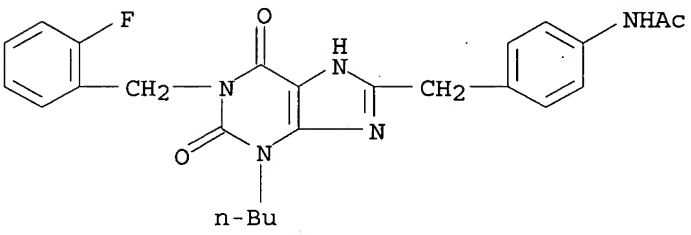
AB The first non-substrate like inhibitors of human cytosolic phosphoenolpyruvate carboxykinase (PEPCK) competitive with GTP are reported. An effort to discover orally active compds. that improve glucose homeostasis in Type 2 diabetics by reversibly inhibiting PEPCK led to the discovery of 1-allyl-3-butyl-8-methylxanthine (5). We now report modifications at N-1 and C-8 that improved the in vitro activity of the initial xanthine HTS hit by 100-fold and a developing SAR for this class of inhibitor.

IT **628279-06-1P 628279-07-2P 628279-08-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(modified dibenzylxanthines as GTP-competitive inhibitors of phosphoenolpyruvate carboxykinase)

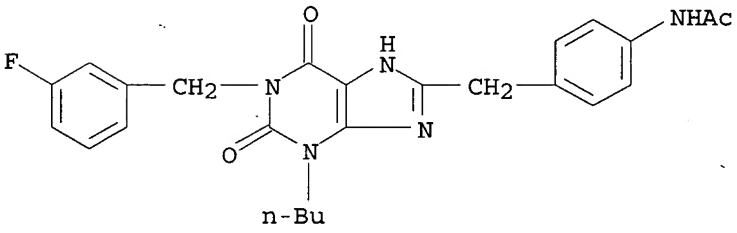
RN 628279-06-1 HCAPLUS
CN Acetamide, N-[4-[[3-butyl-2,3,6,7-tetrahydro-2,6-dioxo-1-(phenylmethyl)-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 628279-07-2 HCAPLUS
CN Acetamide, N-[4-[[3-butyl-1-[(2-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 628279-08-3 HCAPLUS
CN Acetamide, N-[4-[[3-butyl-1-[(3-fluorophenyl)methyl]-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:282400 HCAPLUS
DOCUMENT NUMBER: 138:309280
TITLE: Combinations containing a phosphodiesterase inhibitor
INVENTOR(S): Cohen, David Saul
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft M.B.H.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

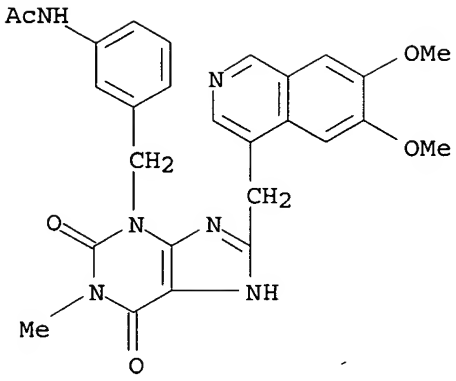
WO 2003028730 A2 20030410 WO 2002-EP10826 20020926
WO 2003028730 A3 20030904
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR
US 2003114469 A1 20030619 US 2002-231427 20020828
US 2003139429 A1 20030724 US 2002-236651 20020906
EP 1432423 A2 20040630 EP 2002-777227 20020926
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
PRIORITY APPLN. INFO.: US 2001-325485P P 20010927
WO 2002-EP10826 W 20020926
OTHER SOURCE(S): MARPAT 138:309280

AB The present invention relates to a pharmaceutical composition, comprising (a) a phosphodiesterase 5 inhibitor or a pharmaceutically acceptable salt thereof and (b) at least one of the active ingredients selected from the group consisting of (i) an anti-diabetic agent; (ii) HMG-Co-A reductase inhibitors; (iii) an antihypertensive agent; and (iv) a serotonin reuptake inhibitor (SSRI) or, in each case, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier. The pharmaceutical composition may be employed for the treatment of sexual dysfunction, hyperglycemia, hyperinsulinemia, hyperlipidemia, hypertriglyceridemia, diabetes, insulin resistance, impaired glucose metabolism, conditions of impaired glucose tolerance (IGT), conditions of impaired fasting plasma glucose, obesity, diabetic retinopathy, diabetic nephropathy, glomerulosclerosis, diabetic neuropathy, syndrome X, erectile dysfunction, coronary heart disease, hypertension, especially ISH, angina pectoris, myocardial infarction, stroke, vascular restenosis, endothelial dysfunction, impaired vascular compliance, congestive heart failure.

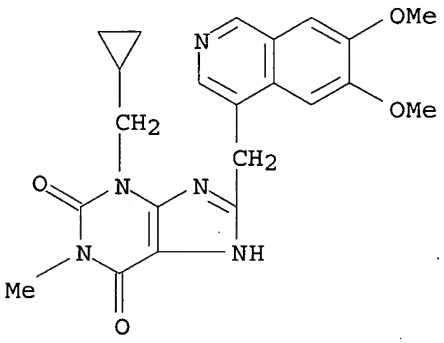
IT **366444-49-7 366444-52-2 366444-55-5**
366444-57-7 366444-60-2 366444-69-1
366444-70-4 366444-71-5 366444-72-6
366444-87-3 366444-88-4 366444-89-5
366444-96-4 366444-97-5 366444-98-6
366444-99-7 366445-00-3 366445-08-1
366445-09-2 366445-10-5 366445-17-2
366445-18-3 366445-19-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. containing PDE5 inhibitor in combination with antidiabetic, HMG-Co-A reductase inhibitor, antihypertensive, or serotonin reuptake inhibitor)

RN 366444-49-7 HCAPLUS

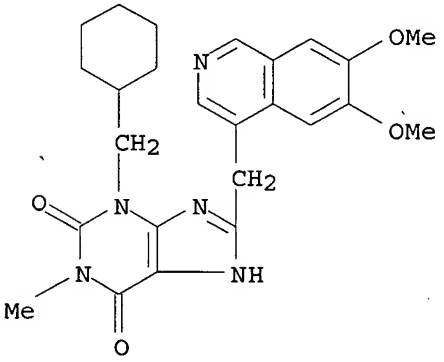
CN Acetamide, N-[3-[[8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



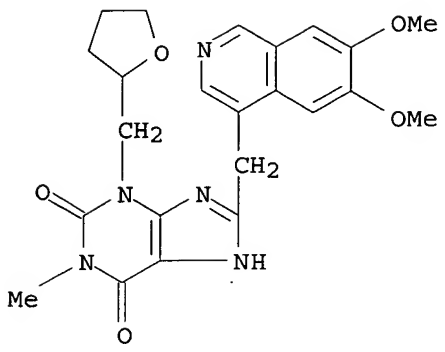
RN 366444-52-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclopropylmethyl)-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



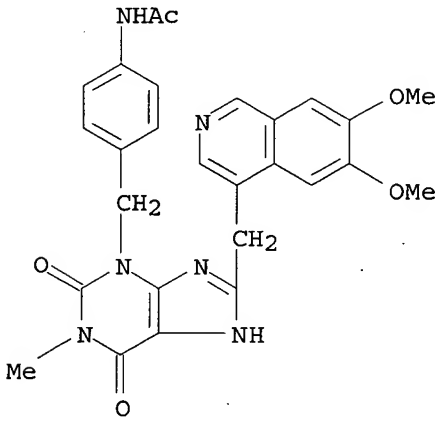
RN 366444-55-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclohexylmethyl)-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



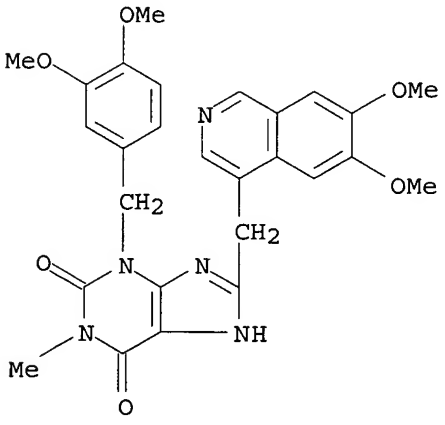
RN 366444-57-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



RN 366444-60-2 HCAPLUS
CN Acetamide, N-[4-[[8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)

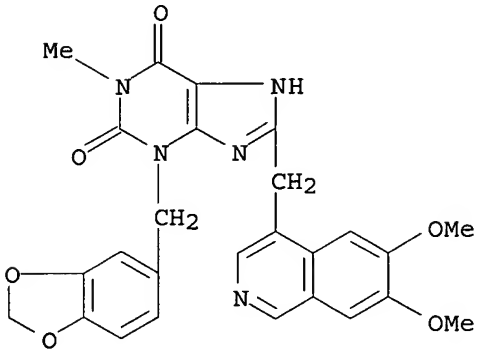


RN 366444-69-1 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3-[(3,4-dimethoxyphenyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)

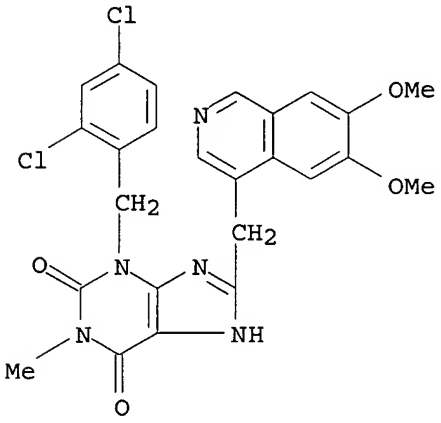


RN 366444-70-4 HCAPLUS

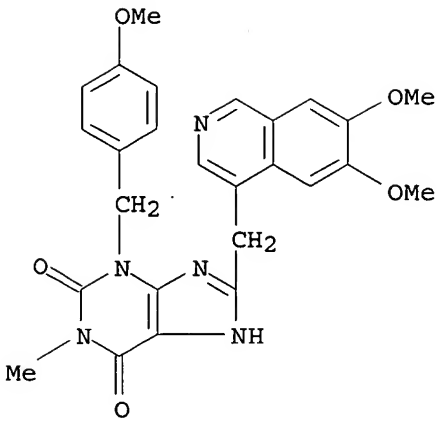
CN 1H-Purine-2,6-dione, 3-(1,3-benzodioxol-5-ylmethyl)-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



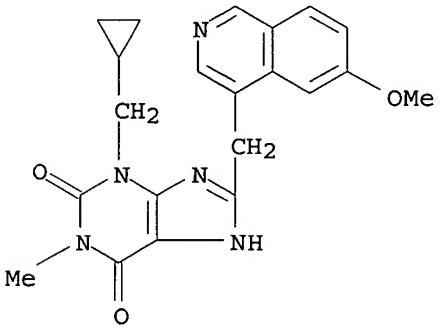
RN 366444-71-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3-[(2,4-dichlorophenyl)methyl]-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



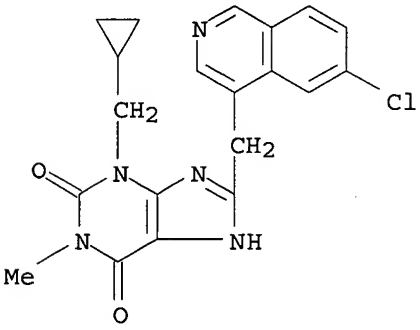
RN 366444-72-6 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-3-[(4-methoxyphenyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



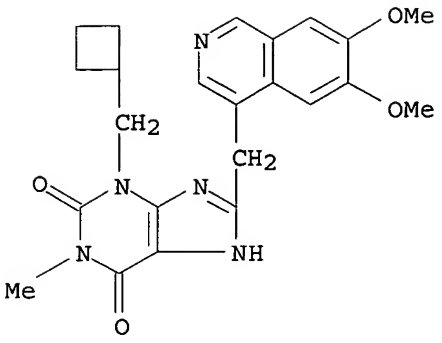
RN 366444-87-3 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclopropylmethyl)-3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



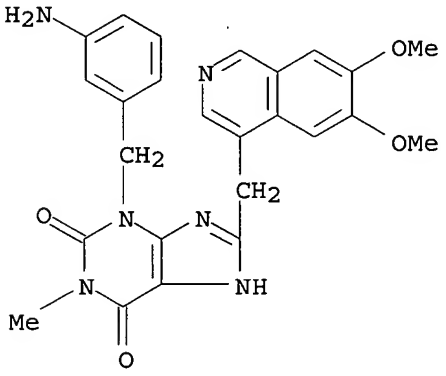
RN 366444-88-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(6-chloro-4-isoquinolinyl)methyl]-3-(cyclopropylmethyl)-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



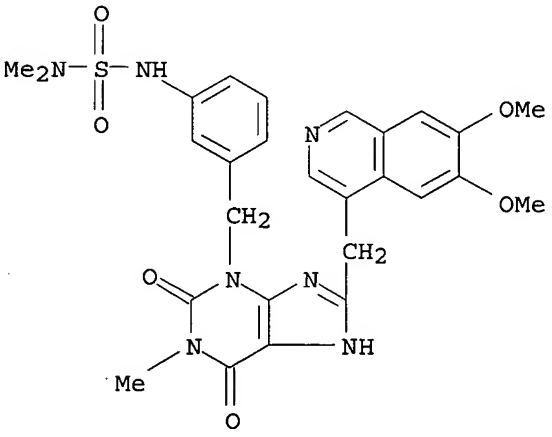
RN 366444-89-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclobutylmethyl)-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 366444-96-4 HCAPLUS
CN 1H-Purine-2,6-dione, 3-[(3-aminophenyl)methyl]-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)

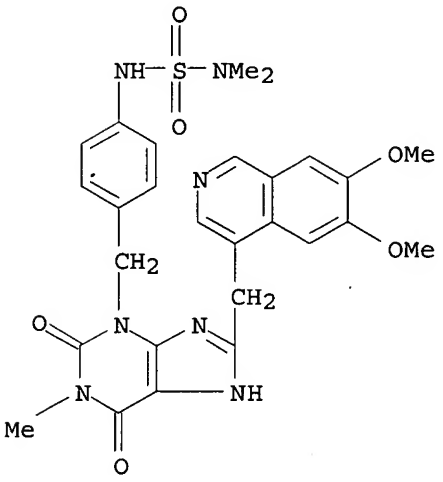


RN 366444-97-5 HCAPLUS
CN Sulfamide, N'-[3-[[8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

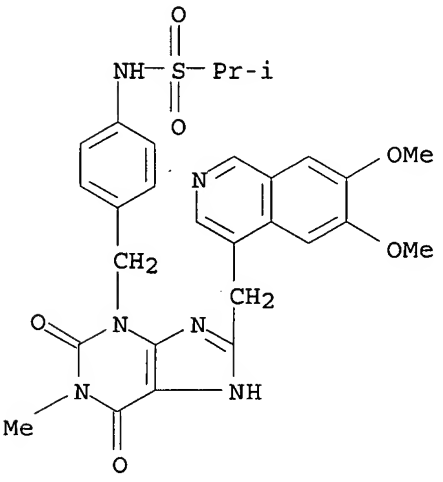


RN 366444-98-6 HCAPLUS

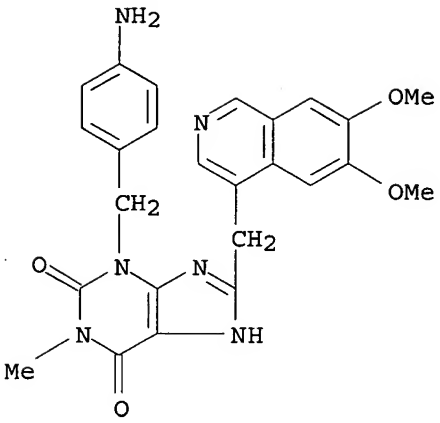
CN Sulfamide, N'-[4-[[8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



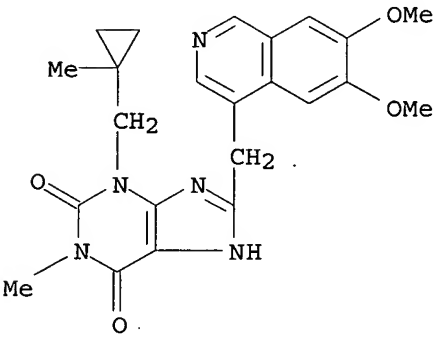
RN 366444-99-7 HCAPLUS
CN 2-Propanesulfonamide, N-[4-[[8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



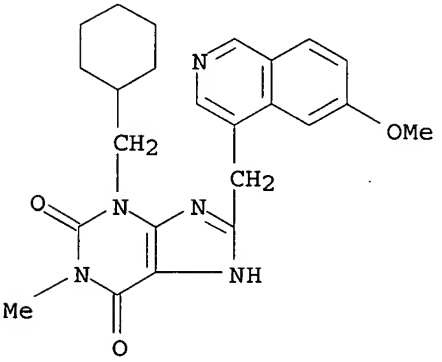
RN 366445-00-3 HCAPLUS
CN 1H-Purine-2,6-dione, 3-[(4-aminophenyl)methyl]-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



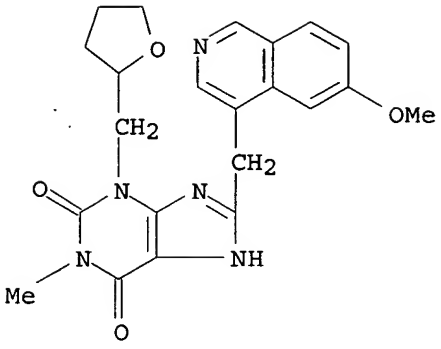
RN 366445-08-1 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-[(1-methylcyclopropyl)methyl]- (9CI) (CA INDEX NAME)



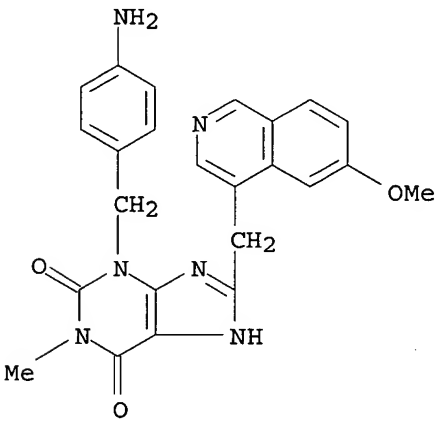
RN 366445-09-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclohexylmethyl)-3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



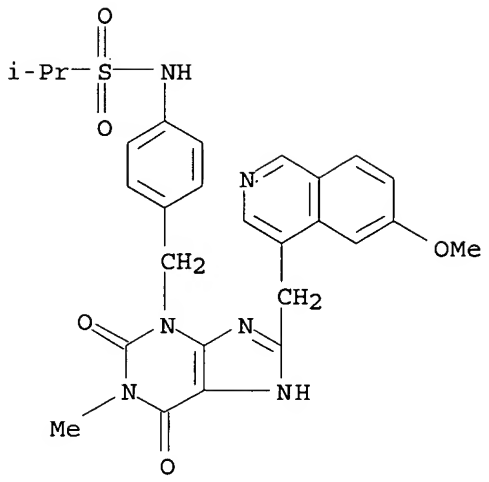
RN 366445-10-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl-3-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



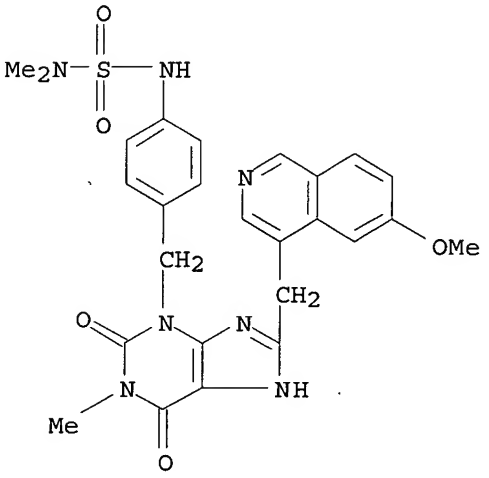
RN 366445-17-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3-[(4-aminophenyl)methyl]-3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



RN 366445-18-3 HCAPLUS
CN 2-Propanesulfonamide, N-[4-[[1,2,6,7-tetrahydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 366445-19-4 HCAPLUS
CN Sulfamide, N,N-dimethyl-N'-[4-[[1,2,6,7-tetrahydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]-(9CI) (CA INDEX NAME)



L20 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:510491 HCAPLUS
DOCUMENT NUMBER: 138:73113
TITLE: A solid-phase approach towards the synthesis of PDE5 inhibitors
AUTHOR(S): Beer, David; Bhalay, Gurdip; Dunstan, Andrew; Glen, Angela; Haberthuer, Sandra; Moser, Heinz
CORPORATE SOURCE: Novartis Horsham Research Centre, RH12 5AB, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(15), 1973-1976
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:73113

AB PDE5 inhibitors based upon the xanthine scaffold have been expediently synthesized using a solid-phase route. Attachment of the xanthine scaffold using the Rink chloride linker and N-1 functionalization using Mitsunobu chemical is described. A library of compds. was produced in multi-milligram quantities with excellent purities and acceptable yields. The compds. were tested for their PDE5 inhibitory activity.

IT **480445-64-5P 480445-66-7P 480445-74-7P 480445-76-9P 480445-78-1P 480445-84-9P 480445-86-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solid-phase approach towards the synthesis of xanthine derivs. as PDE5 inhibitors)

RN 480445-64-5 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(4-bromophenyl)methyl]-1-(cyclobutylmethyl)-3,7-dihydro-3-(2-methylpropyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

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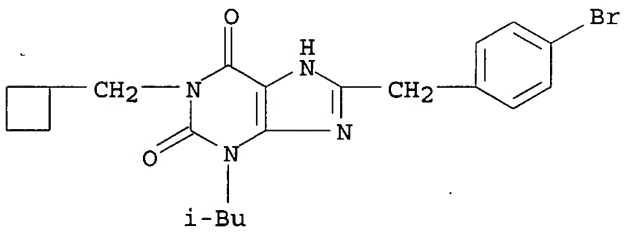
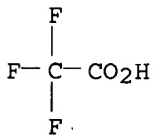
CRN 480445-63-4
CMF C21 H25 Br N4 O2



CM 2

CRN 76-05-1
CMF C2 H F3 O2

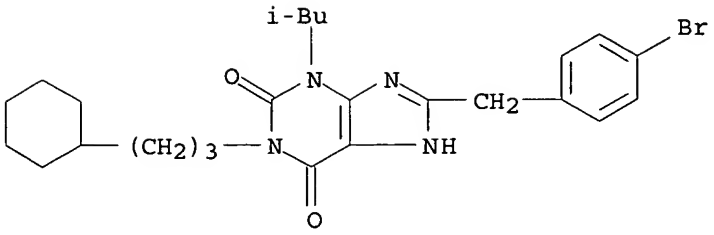


RN 480445-66-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(4-bromophenyl)methyl]-1-(3-cyclohexylpropyl)-3,7-dihydro-3-(2-methylpropyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

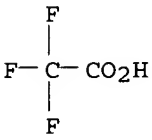
CM 1

CRN 480445-65-6
CMF C25 H33 Br N4 O2



CM 2

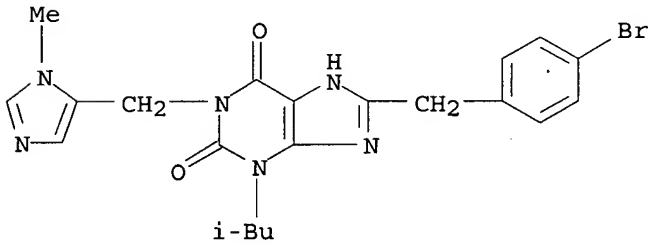
CRN 76-05-1
CMF C2 H F3 O2



RN 480445-74-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(4-bromophenyl)methyl]-3,7-dihydro-1-[(1-methyl-1H-imidazol-5-yl)methyl]-3-(2-methylpropyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

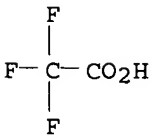
CM 1

CRN 480445-73-6
CMF C21 H23 Br N6 O2



CM 2

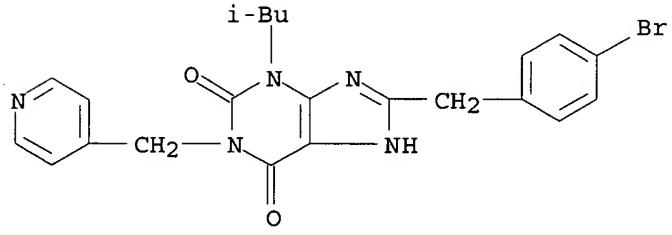
CRN 76-05-1
CMF C2 H F3 O2



RN 480445-76-9 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(4-bromophenyl)methyl]-3,7-dihydro-3-(2-methylpropyl)-1-(4-pyridinylmethyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

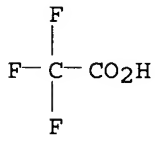
CM 1

CRN 480445-75-8
CMF C22 H22 Br N5 O2



CM 2

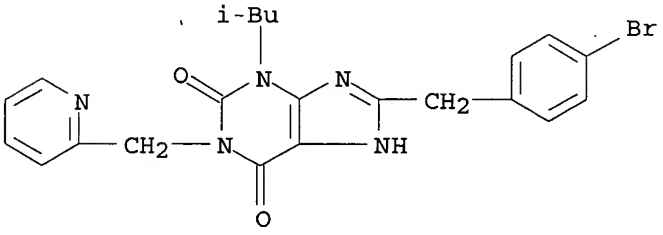
CRN 76-05-1
CMF C2 H F3 O2



RN 480445-78-1 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(4-bromophenyl)methyl]-3,7-dihydro-3-(2-methylpropyl)-1-(2-pyridinylmethyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

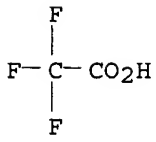
CM 1

CRN 480445-77-0
CMF C22 H22 Br N5 O2



CM 2

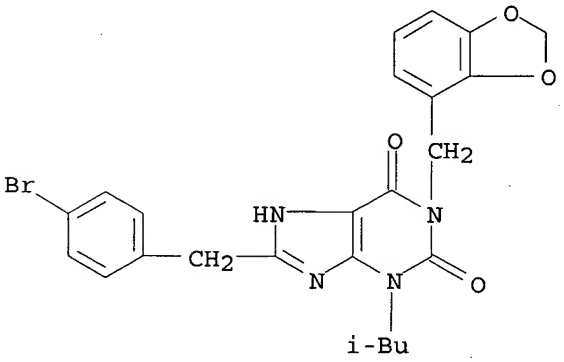
CRN 76-05-1
CMF C2 H F3 O2



RN 480445-84-9 HCAPLUS
CN 1H-Purine-2,6-dione, 1-(1,3-benzodioxol-4-ylmethyl)-8-[(4-bromophenyl)methyl]-3,7-dihydro-3-(2-methylpropyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

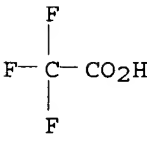
CM 1

CRN 480445-83-8
CMF C24 H23 Br N4 O4



CM 2

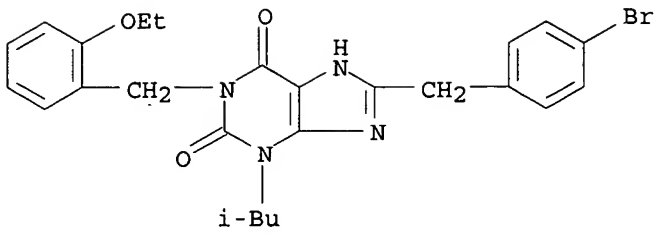
CRN 76-05-1
CMF C2 H F3 O2



RN 480445-86-1 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(4-bromophenyl)methyl]-1-[(2-ethoxyphenyl)methyl]-3,7-dihydro-3-(2-methylpropyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

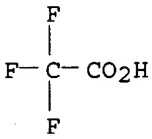
CM 1

CRN 480445-85-0
CMF C25 H27 Br N4 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:762998 HCAPLUS
DOCUMENT NUMBER: 135:303908
TITLE: 8-(Quinolinylmethyl)xanthine and 8-(isoquinolinylmethyl)xanthine derivatives as PDE 5 inhibitors, useful for treatment of erectile dysfunction
INVENTOR(S): Bhalay, Gurdip; Collingwood, Stephen Paul; Fairhurst, Robin Alec; Gomez, Sylvie Felicite; Naef, Reto; Sandham, David Andrew
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077110	A1	20011018	WO 2001-EP3909	20010405

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001073921	A5	20011023	AU 2001-73921	20010405
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JP 2003530398	T2	20031014	JP 2001-575583	20010405
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PT 1268480	T	20040331	PT 2001-940294	20010405
NZ 521361	A	20040528	NZ 2001-521361	20010405
ES 2210169	T3	20040701	ES 2001-1940294	20010405
NO 2002004741	A	20021002	NO 2002-4741	20021002
US 2003171384	A1	20030911	US 2002-240481	20021002
ZA 2002007956	A	20030716	ZA 2002-7956	20021003
US 2004038996	A1	20040226	US 2003-644328	20030820
PRIORITY APPLN. INFO.:			GB 2000-8694 A	20000407
			WO 2001-EP3909 W	20010405
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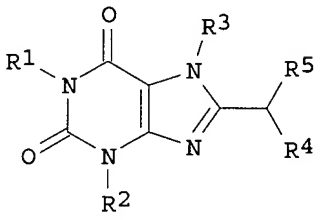
OTHER SOURCE(S): MARPAT 135:303908

GI



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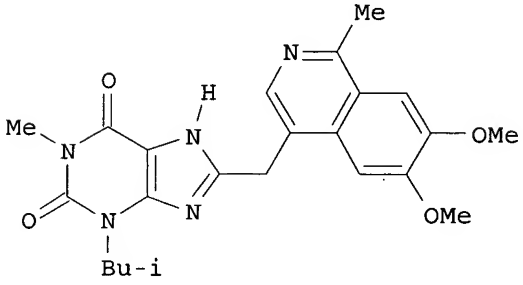


II

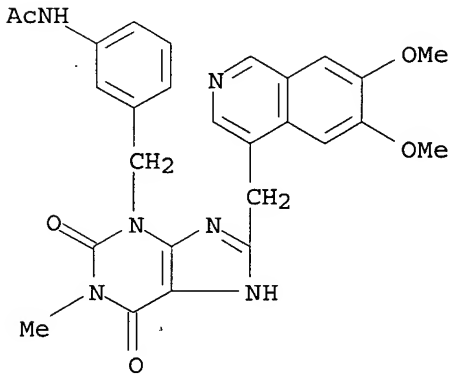
AB Compds. of formula I, in free or salt form, are disclosed [where R1 = H or alkyl (un)substituted by OH, alkoxy, or alkylthio; R2 = H, alkyl, hydroxyalkyl, alkylcarbonyloxyalkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, cycloalkylalkyl, heterocyclylalkyl, aralkyl [aryl ring optionally fused to 5-membered heterocyclic group or substituted by alkoxy, (di)(alkyl)amino, acylamino, halo, OH, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, alkylsulfonylamino or dialkylaminosulfonylamino]; R3 = H or alkyl optionally substituted by OH, alkoxy, or alkylthio; R4 = H or alkyl; R5 = (un)substituted quinolinyl, isoquinolinyl, or oxodihydroisoquinolinyl, optionally fused to 5-membered heterocyclic group [substituents = halo, cyano, OH, alkyl, hydroxyalkyl, alkoxyalkyl, alkylthioalkyl, alkoxy, alkylthio, alkenyl, alkoxycarbonyl, alkynyl, carboxyl, acyl, N(R6)R7, (un)substituted aryl (substituents = halo or alkoxy), or 5- or 6-membered heteroaryl attached through ring C]; R6, R7 = H or alkyl (optionally substituted by OH or alkoxy); or 1 of R6 and R7 = H, the other = acyl; or NR6R7 = 5- or 6- membered heterocyclyl]. I are

inhibitors of cGMP phosphodiesterases (PDEs), and in particular are selective inhibitors of PDE5. They exhibit good selectivity for PDE5 over PDE1 and PDE6, indicating a low side-effect profile. I are of particular interest for use in the treatment of sexual dysfunction, especially male erectile dysfunction. Examples include 87 product syntheses and 59 intermediate prepns. Ten compds. are particularly preferred, and these are specifically claimed. For instance, cyclocondensation of 5,6-diamino-1-isobutyl-3-methyl-1H-pyrimidine-2,4-dione with (6,7-dimethoxy-1-methylisoquinolin-4-yl)acetic acid (prepns. given), using EDC in aqueous MeOH, gave the preferred title compound II. In an in vitro assay for PDE5 inhibition, I gave IC50 values of 0.0005 μM to 10 μM, e.g., 0.007 μM for II.

IT **366444-49-7P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-[[3-(acetylamino)phenyl]methyl]-1-methyl-3,7-dihydropurine-2,6-dione
366444-96-4P, 3-(3-Aminobenzyl)-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of quinoline-xanthine and isoquinoline-xanthine derivs. as PDE 5 inhibitors)

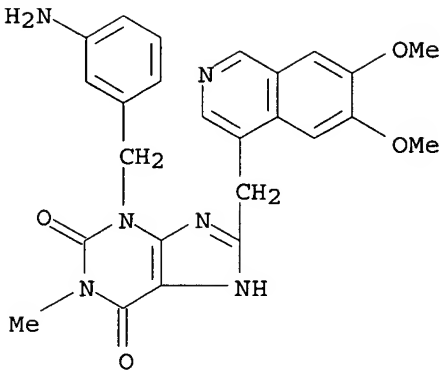
RN 366444-49-7 HCAPLUS

CN Acetamide, N-[3-[[8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 366444-96-4 HCAPLUS

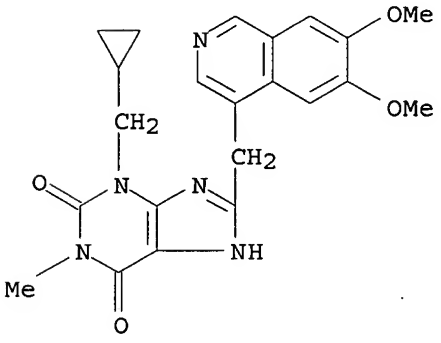
CN 1H-Purine-2,6-dione, 3-[(3-aminophenyl)methyl]-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



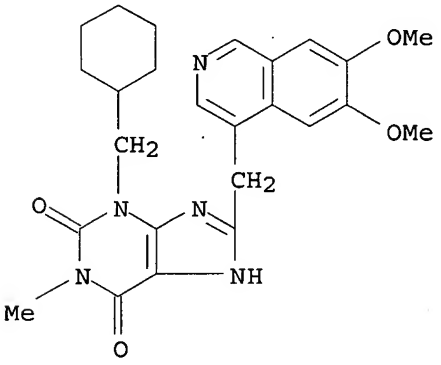
IT **366444-52-2P**, 3-(Cyclopropylmethyl)-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366444-55-5P**, 3-(Cyclohexylmethyl)-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366444-57-7P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3-(tetrahydrofurfuryl)-3,7-dihydropurine-2,6-dione **366444-60-2P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-[[4-(acetylamino)phenyl]methyl]-1-methyl-3,7-dihydropurine-2,6-dione **366444-69-1P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-(3,4-dimethoxybenzyl)-1-methyl-3,7-dihydropurine-2,6-dione **366444-70-4P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-(3,4-methylenedioxybenzyl)-1-methyl-3,7-dihydropurine-2,6-dione **366444-71-5P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-(2,4-dichlorobenzyl)-1-methyl-3,7-dihydropurine-2,6-dione **366444-72-6P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-(4-methoxybenzyl)-1-methyl-3,7-dihydropurine-2,6-dione **366444-87-3P**, 8-(6-Methoxyisoquinolin-4-ylmethyl)-3-(cyclopropylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366444-88-4P**, 8-(6-Chloroisoquinolin-4-ylmethyl)-3-(cyclopropylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366444-89-5P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-(cyclobutylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366444-97-5P**, 3-[3-[(N,N-Dimethylsulfamoyl)amino]benzyl]-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366444-98-6P**, 3-[4-[(N,N-Dimethylsulfamoyl)amino]benzyl]-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366444-99-7P**, 3-[4-[[(1-Methylethyl)sulfonyl]amino]benzyl]-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366445-00-3P**, 3-(4-Aminobenzyl)-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366445-08-1P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3-[(1-methylcyclopropyl)methyl]-3,7-dihydropurine-2,6-dione **366445-09-2P**, 8-(6-Methoxyisoquinolin-4-ylmethyl)-3-(cyclohexylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366445-10-5P**, 8-(6-Methoxyisoquinolin-4-ylmethyl)-3-(tetrahydrofurfuryl)-1-methyl-3,7-dihydropurine-2,6-dione **366445-17-2P**, 3-(4-Aminobenzyl)-8-(6-methoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366445-18-3P**, 3-[4-[[(1-Methylethyl)sulfonyl]amino]benzyl]-8-(6-methoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366445-19-4P**, 3-[4-[[(N,N-Dimethylamino)sulfonyl]amino]benzyl]-8-(6-methoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366446-18-6P**, 3-(3-Aminobenzyl)-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione dihydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinoline-xanthine and isoquinoline-xanthine derivs. as PDE 5 inhibitors)

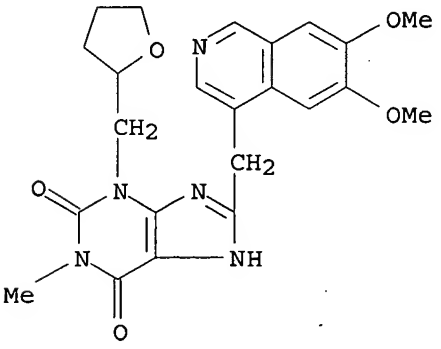
RN 366444-52-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclopropylmethyl)-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



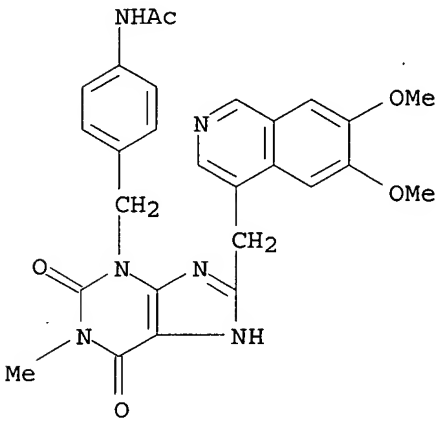
RN 366444-55-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclohexylmethyl)-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



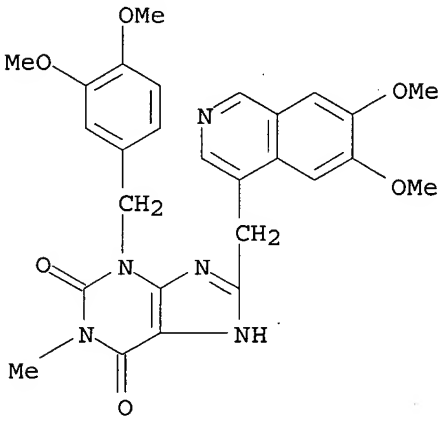
RN 366444-57-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



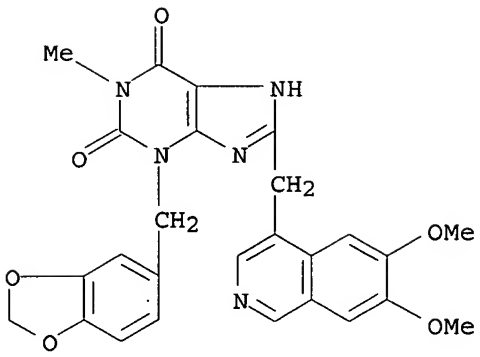
RN 366444-60-2 HCAPLUS
CN Acetamide, N-[4-[[8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



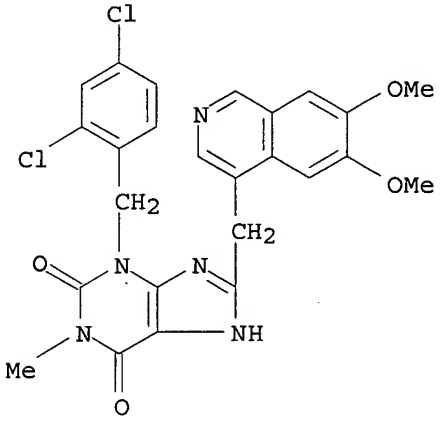
RN 366444-69-1 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3-[(3,4-dimethoxyphenyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



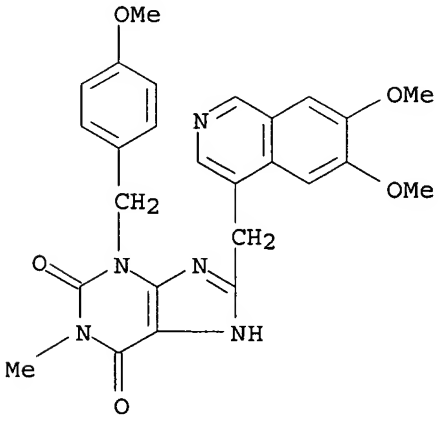
RN 366444-70-4 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(1,3-benzodioxol-5-ylmethyl)-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



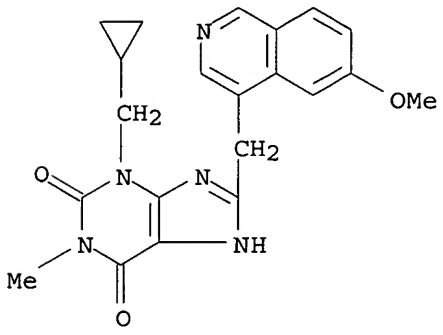
RN 366444-71-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3-[(2,4-dichlorophenyl)methyl]-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



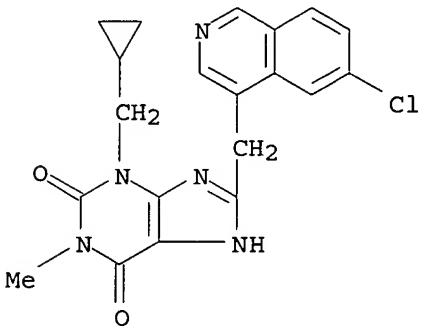
RN 366444-72-6 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-3-[(4-methoxyphenyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



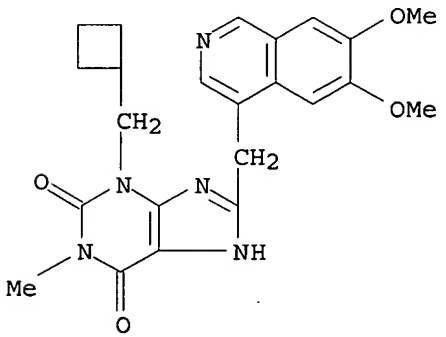
RN 366444-87-3 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclopropylmethyl)-3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



RN 366444-88-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(6-chloro-4-isoquinolinyl)methyl]-3-(cyclopropylmethyl)-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)

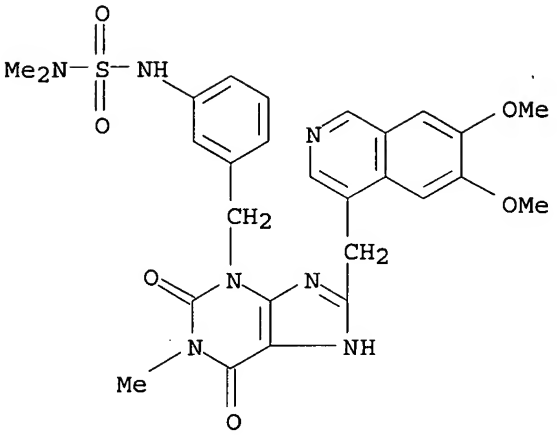


RN 366444-89-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclobutylmethyl)-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)

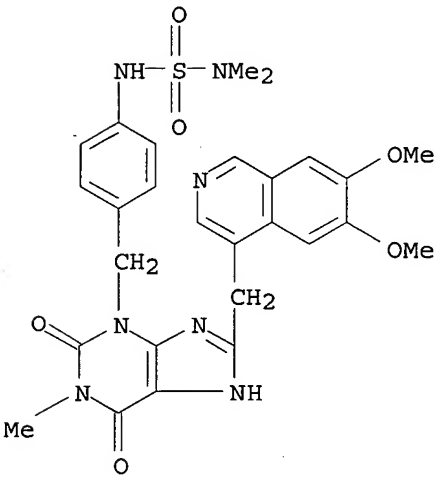


RN 366444-97-5 HCAPLUS
CN Sulfamide, N'-[3-[[8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]-N,N-dimethyl-

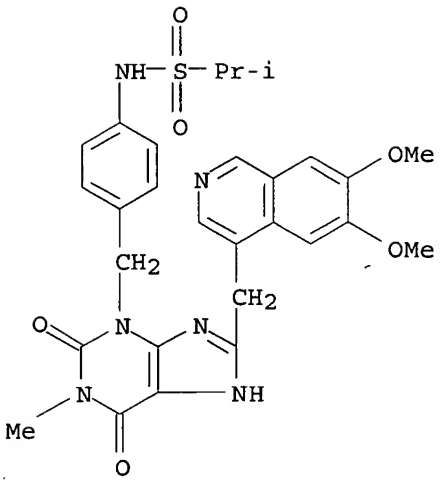
(9CI) (CA INDEX NAME)



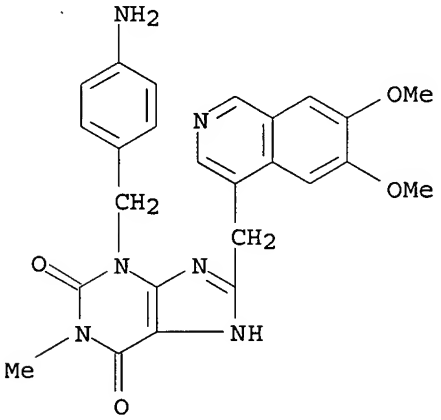
RN 366444-98-6 HCAPLUS
CN Sulfamide, N'-[4-[[8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



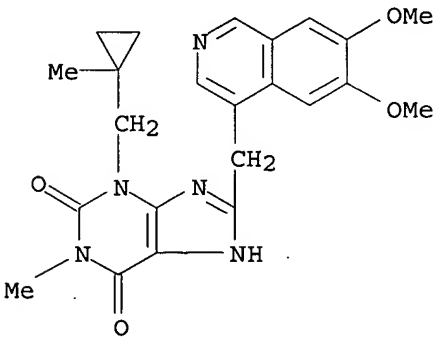
RN 366444-99-7 HCAPLUS
CN 2-Propanesulfonamide, N-[4-[[8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



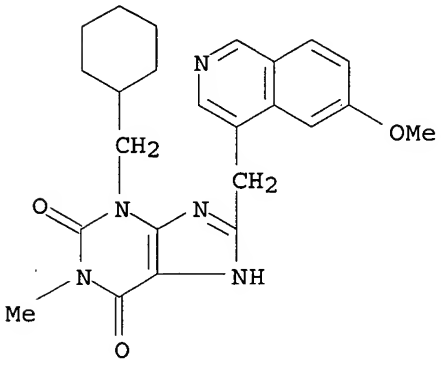
RN 366445-00-3 HCAPLUS
CN 1H-Purine-2,6-dione, 3-[(4-aminophenyl)methyl]-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



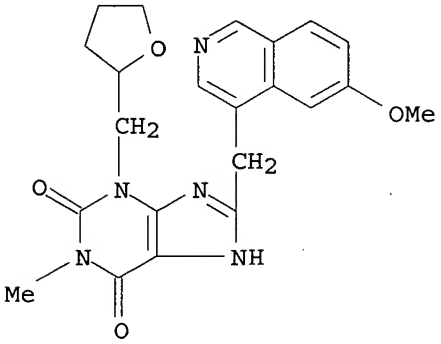
RN 366445-08-1 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-[(1-methylcyclopropyl)methyl]- (9CI) (CA INDEX NAME)



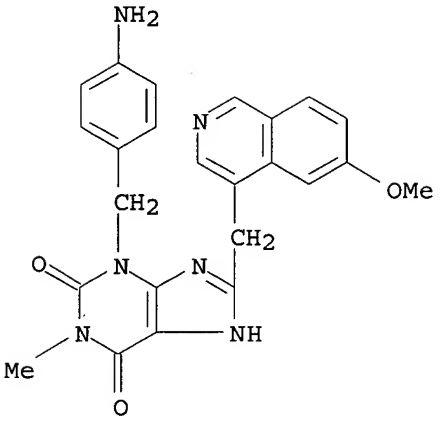
RN 366445-09-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3-(cyclohexylmethyl)-3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



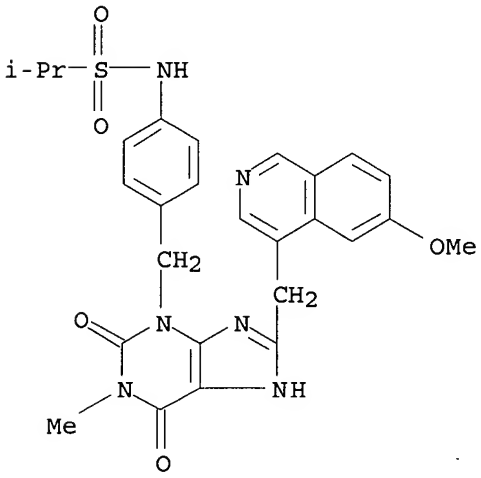
RN 366445-10-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl-3-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



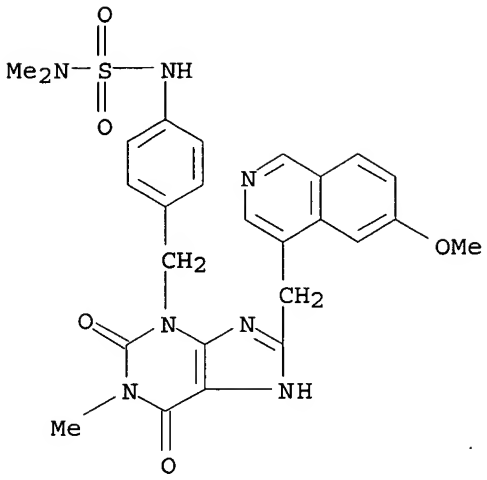
RN 366445-17-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3-[(4-aminophenyl)methyl]-3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



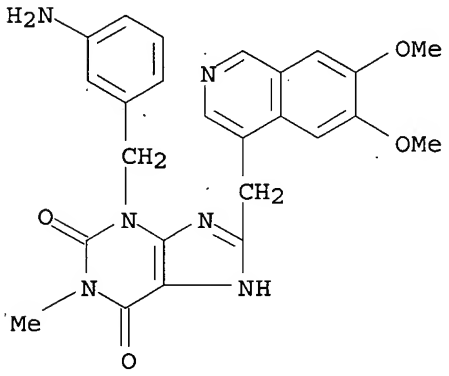
RN 366445-18-3 HCAPLUS
CN 2-Propanesulfonamide, N-[4-[[1,2,6,7-tetrahydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 366445-19-4 HCAPLUS
CN Sulfamide, N,N-dimethyl-N'-[4-[[1,2,6,7-tetrahydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 366446-18-6 HCAPLUS
CN 1H-Purine-2,6-dione, 3-[(3-aminophenyl)methyl]-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-, dihydrochloride (9CI) (CA INDEX NAME)



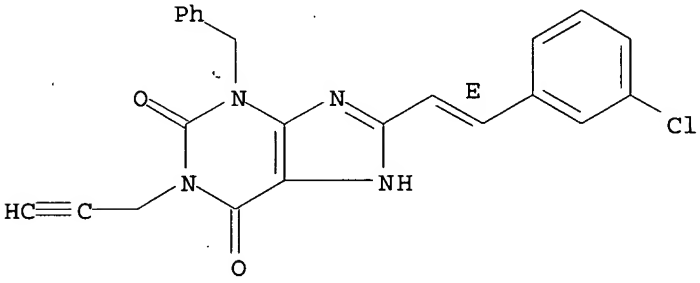
●2 HCl

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:933405 HCAPLUS
DOCUMENT NUMBER: 124:202706
TITLE: A new versatile synthesis of xanthines with variable substituents in the 1-, 3-, 7-, and 8-positions
AUTHOR(S): Mueller, Christa E.; Sandoval-Ramirez, Jesus
CORPORATE SOURCE: Inst. Pharmazie Lebensmittelchemie, Univ. Wuerzburg, Wuerzburg, D-97074, Germany
SOURCE: Synthesis (1995), (10), 1295-9
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Thieme
DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 124:202706
AB A new convenient procedure for the synthesis of a wide range of xanthines was developed starting from 3-substituted 6-aminouraciles. Nitrosation and reduction yields the corresponding 5,6-diaminouracils, which are condensed with carboxylic acids. The resulting amides can be selectively alkylated at the uracil ring N(1), corresponding to xanthine N(3), under mild conditions. Ring closure and, if desired, alkylation at the 7-position, yields di-, tri-, or tetrasubstituted xanthines in high yields. Sensitive substituents, such as prop-2-ynyl, can be introduced in the 1-position. Variation of the 3-substituent is considerably facilitated in comparison with the standard procedure for the preparation of xanthines.
IT **174519-11-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of xanthines)
RN 174519-11-0 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[2-(3-chlorophenyl)ethenyl]-3,7-dihydro-3-(phenylmethyl)-1-(2-propynyl)-, (E)- (9CI) (CA INDEX NAME)

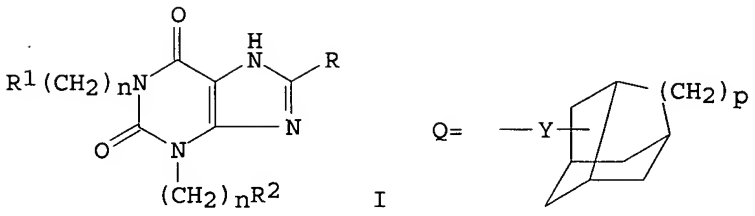
Double bond geometry as shown.



L20 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:107052 HCAPLUS
DOCUMENT NUMBER: 120:107052
TITLE: Diuretic xanthine derivatives having a high sodium excretion factor
INVENTOR(S): Suzuki, Fumio; Shimada, Junichi; Karasawa, Akira; Mizumoto, Hideaki; Kase, Hiroshi; Nonaka, Hiromi
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 560354	A1	19930915	EP 1993-103926	19930311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 06016668	A2	19940125	JP 1993-49652	19930310
US 5342841	A	19940830	US 1993-29069	19930310
CA 2091553	AA	19930913	CA 1993-2091553	19930311
PRIORITY APPLN. INFO.:			JP 1992-53385	19920312

OTHER SOURCE(S): MARPAT 120:107052
GI



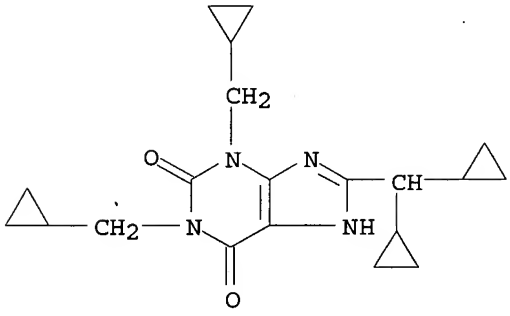
I

AB The title compds. I [R = Q, CHR3R4; R3, R4 = (un)substituted alicyclic alkyl; Y = direct bond, alkylene; p = 0, 1; R1, R2 = (un)substituted alicyclic alkyl; m, n = 0-2], which demonstrate diuretic activity, are prepared and I-containing formulations presented. Thus, 3-noradamantanecarboxylic acid was condensed with 5,6-diamino-1,3-bis(cyclopropylmethyl)uracil, and the intermediate carbonylaminouracil intramolecularly cyclocondensed, producing 1,3-bis(cyclopropylmethyl)-8-(3-noradamantyl)xanthine (II). When administered to male rats at 0.1 mg/kg, II produced a 184% increase in volume of excreted urine, vs. 75% for furosemide administered at 25 mg/kg.

IT **152534-50-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and diuretic activity of)

RN 152534-50-4 HCAPLUS

CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-8-(dicyclopropylmethyl)-3,7-dihydro- (9CI) (CA INDEX NAME)



L20 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1993:559990 HCAPLUS

DOCUMENT NUMBER: 119:159990

TITLE: Preparation of 8-cycloalkylxanthines as psychoanaleptics

INVENTOR(S): Fumio, Suzuki; Junichi, Shimada; Hiromasa, Kato; Akio, Ishii; Shizuo, Shiozaki

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

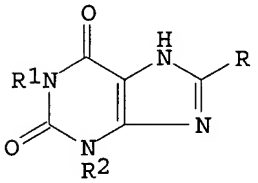
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 541120	A2	19930512	EP 1992-119080	19921106
EP 541120	A3	19930721		
EP 541120	B1	19990526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 05194516	A2	19930803	JP 1992-295094	19921104
JP 3115128	B2	20001204		
CA 2082325	AA	19930509	CA 1992-2082325	19921106
AT 180482	E	19990615	AT 1992-119080	19921106
US 5447933	A	19950905	US 1992-973959	19921109
PRIORITY APPLN. INFO.:			JP 1991-293269 A	19911108
OTHER SOURCE(S):	MARPAT 119:159990			

GI



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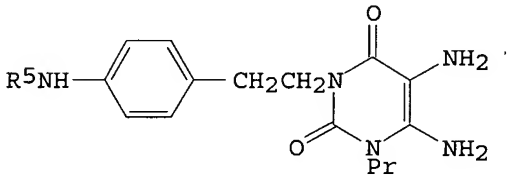


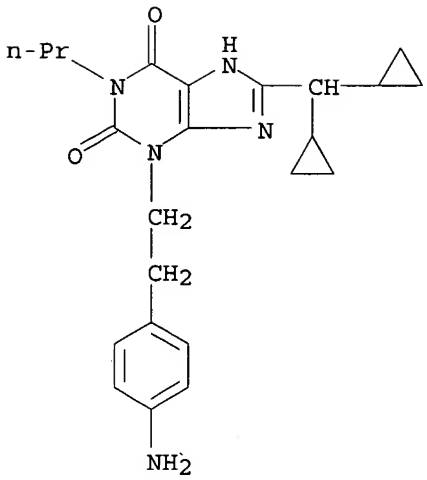
II

AB Title compds. I [R = CHR3R4, di- or tricycloalkyl(alkyl); 1 of R1,R2 = (CH2)mX and the other alkyl, alkenyl, Ph, CH2Ph, etc.; R3,R4 = (substituted) cycloalkyl; X = amino(hetero)aryl; m = 2 or 3] were prepared Thus, diaminouracil II (R5 = CO2CH2Ph) (preparation given) was condensed with dicyclopropylacetc acid and the deprotected product cyclized to give I [R = dicyclopropylmethyl, R1 = 4-(H2N)C6H4CH2CH2, R2 = Pr] which gave 216 s latent reaction time (control = 44 s) in scopolamine-treated rats at 0.08 mg/kg orally.

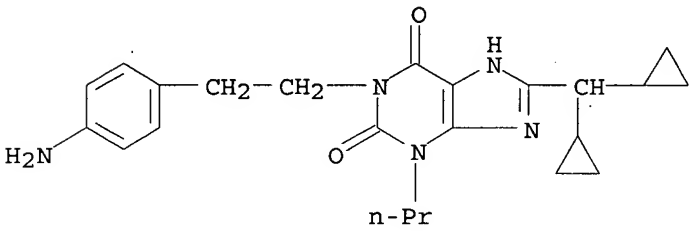
IT **149741-44-6P 149741-45-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as psychoanaleptic)

RN 149741-44-6 HCAPLUS

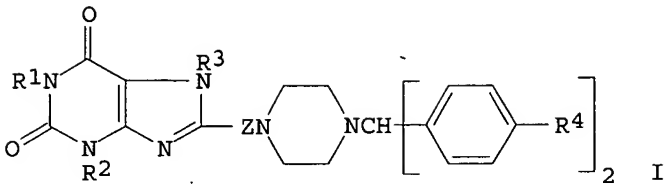
CN 1H-Purine-2,6-dione, 3-[2-(4-aminophenyl)ethyl]-8-(dicyclopropylmethyl)-3,7-dihydro-1-propyl- (9CI) (CA INDEX NAME)



RN 149741-45-7 HCAPLUS
CN 1H-Purine-2,6-dione, 1-[2-(4-aminophenyl)ethyl]-8-(dicyclopropylmethyl)-3,7-dihydro-3-propyl- (9CI) (CA INDEX NAME)



L20 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:628857 HCAPLUS
DOCUMENT NUMBER: 107:228857
TITLE: New xanthine derivatives with potent and long lasting anti-bronchoconstrictive activity
AUTHOR(S): Regnier, Gilbert L.; Guillonneau, Claude G.; Duhault, Jacques L.; Tisserand, Francoise P.; Saint-Romas, Guy; Holstorp, Sophie M.
CORPORATE SOURCE: Chem. Res. Dep., Inst. Rech. Servier, Suresnes, 92150, Fr.
SOURCE: European Journal of Medicinal Chemistry (1987), 22(3), 243-50
CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 107:228857
GI



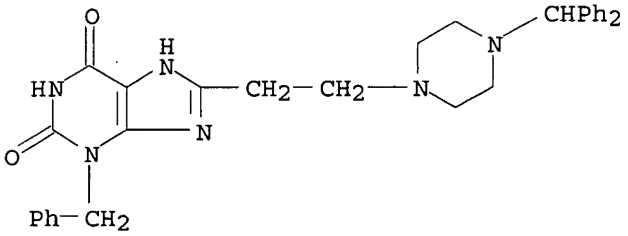
I

AB Twenty-nine new derivs. of 8-aminoalkyl-substituted xanthine [e.g. I, R1 = H, Me, Et; R2 = Me, iso-Pr, Ph, etc.; R3 = H, Me, 2,3-dihydroxypropyl, etc.; R4 = H or F; and X = CH(OH)CH2, (CH2)n; n = 1-3] were synthesized. All I demonstrated a potent anti-bronochoconstrictive effect in the guinea pig and some had a very long duration of action (> 48h). II was selected for clin. trials in asthmatic patients because of its long duration of action, its lack of central nervous system-stimulating effects and its inhibiting action on mast cell degranulation and phosphodiesterse activity. Structure-activity relationships are discussed.

IT **110480-49-4P**
RL: ADV (Adverse effect, including toxicity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and bronchodilating activity and toxicity of)

RN 110480-49-4 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



L20 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1985:578277 HCAPLUS

DOCUMENT NUMBER: 103:178277

TITLE: Xanthine derivatives and pharmaceutical compositions containing them

INVENTOR(S): Regnier, Gilbert; Guillonneau, Claude; Duhault, Jacques; Roman, Francois

PATENT ASSIGNEE(S): ADIR, Fr.

SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

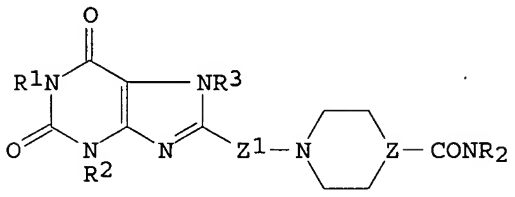
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 149578	A2	19850724	EP 1985-400072	19850116
EP 149578	A3	19850918		
EP 149578	B1	19890125		

R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
FR 2558162	A1	19850719	FR 1984-659	19840117
FR 2558162	B1	19860425		
US 4599338	A	19860708	US 1985-692049	19850116
CA 1228353	A1	19871020	CA 1985-472209	19850116
AT 40368	E	19890215	AT 1985-400072	19850116
AU 8537756	A1	19850725	AU 1985-37756	19850117
AU 569983	B2	19880225		
ZA 8500388	A	19850828	ZA 1985-388	19850117
JP 60174788	A2	19850909	JP 1985-6649	19850117
JP 04015792	B4	19920319		
ES 539658	A1	19860401	ES 1985-539658	19850117
PRIORITY APPLN. INFO.:			FR 1984-659	19840117
			EP 1985-400072	19850116

OTHER SOURCE(S): CASREACT 103:178277

GI



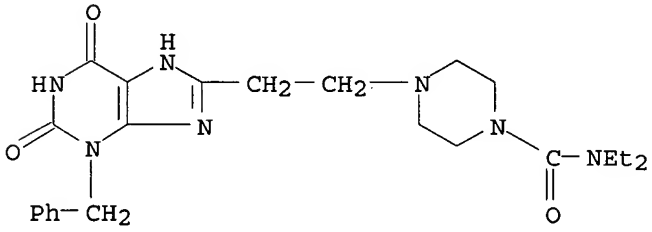
I

AB 8-Substituted xanthines I [R = alkyl, NR2 form a heterocycle; Z = N, CHNH; Z1 = (CH2)n (n = 1,2,3,4), hydroxyalkylene; R1 = H, alkyl; R2 = H, alkyl, alkenyl, PhCH2; R3 = H, Me], which were prepared, are useful in the treatment of migraine and asthenia (no data). 8-(3-Bromopropyl)-1,3,7-trimethylxanthine was treated with 1-(diethylcarbamoyl)piperazine to give I [R = Et, Z = N, Z1 = (CH2)3, R1 = R2 = R3 = Me].

IT **98834-03-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrogenolysis of)

RN 98834-03-8 HCAPLUS

CN 1-Piperazinecarboxamide, N,N-diethyl-4-[2-[2,3,6,7-tetrahydro-2,6-dioxo-3-(phenylmethyl)-1H-purin-8-yl]ethyl]- (9CI) (CA INDEX NAME)



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